EFFECT OF BODY MASS INDEX AND WAIST CIRCUMFERENCE ON RENAL FUNCTION IN HYPERTENSIVE CHRONIC KIDNEY DISEASE

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the

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(M.D. PHYSIOLOGY)

BRANCH-V

THANJAVUR MEDICAL COLLEGE HOSPITAL

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CHENNAI, INDIA

APRIL - 2017

CERTIFICATE

This dissertation entitled **"EFFECT OF BODY MASS INDEX AND WAIST CIRCUMFERENCE ON RENAL FUNCTION IN HYPERTENSIVE CHRONIC KIDNEY DISEASE"** is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the regulations for the award of M.D., Degree in physiology in the Examinations to be held during April 2017.

This Dissertation is a record of fresh work done by the candidate Dr.J.ROSE PRIYADHARSHINI, during the course of the study (2014-2017). This work was carried out by the candidate herself under my supervision.

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I solemnly declare that the Dissertation titled **"EFFECT OF BODY MASS INDEX AND WAIST CIRCUMFERENCE ON RENAL FUNCTION IN HYPERTENSIVE CHRONIC KIDNEY DISEASE"** is done by me at Thanjavur Medical College, Thanjavur

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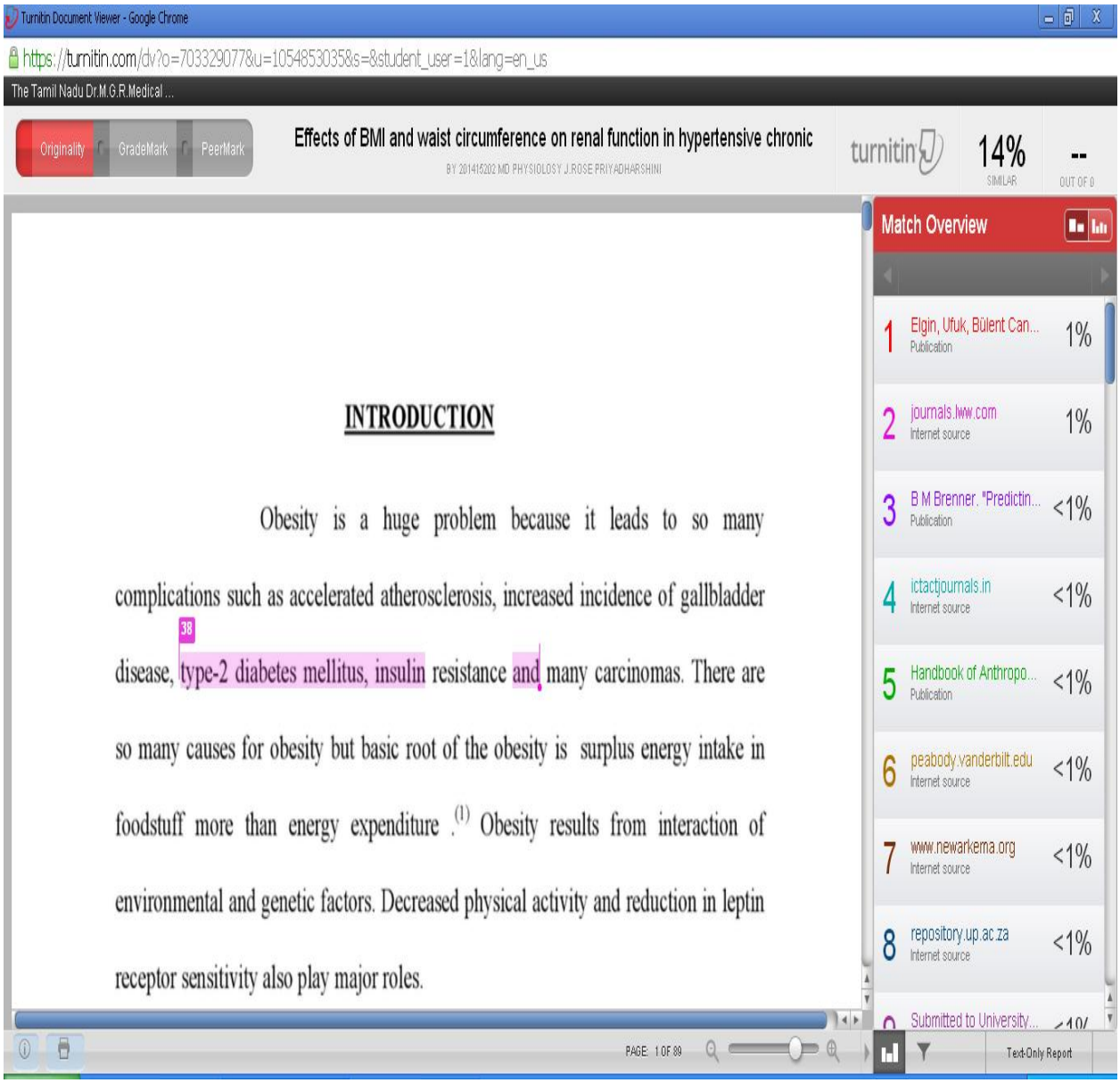

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EFFECT OF BODY MASS INDEX AND WAIST CIRCUMFERENCE ON RENAL FUNCTION IN HYPERTENSIVE CHRONIC KIDNEY DISEASE

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INTRODUCTION

Obesity is a huge problem because it leads to so many complications such as accelerated atherosclerosis, increased incidence of gallbladder disease, type-2 diabetes mellitus, insulin resistance and many carcinomas. There are so many causes for obesity but basic root of the obesity is surplus energy intake in foodstuff more than energy expenditure .[1] Obesity results from interaction of environmental and genetic factors. Decreased physical activity and reduction in leptin receptor sensitivity also play major roles.

There are three important anthropometric dimensions for instance weight, height, waist circumference (WC) in the evaluation of obesity degree.[2,3] Body Mass Index (BMI) is derived by dividing the weight by height, BMI = Wt (Kilograms) / Ht (meter^2),which estimates body fat.BMI cannot differentiate between fat stack and lean body mass or muscle mass. Excess abdominal fat is measured by WC and waist hip ratio (WHR) .[3]

Obese individuals are at risk of early death from various complications. Men with 10 % overweight have 13 percentage greater hazard of death and who are with 20 percentage overweight the risk is increased to 25 percentage.[3]

Various studies suggested that surfeit weight gain is a key risk aspect for hypertension .[4,5,6,7] For every 10 Kg in body weight there was three mmHg climb in systolic bloodpressure and 2.3 mmHg increase in diastolic bloodpressure (DBP) explained by INTERSALT study.[3] WC,BMI,WHR are strongly linked to

bloodpressure. [5,8]Various studies suggested that decline in weight leads to bloodpressure reduction.[2,9-12]

Hypertension is prevalent all over the world and target major organs of the body leading to coronary heart disease, cerebrovascular disease, kidney damage etc. Approximately 10 – 15 % population is suffered from hypertension. 5–20 % ESRD is due to hypertension [13] .Kidney is a target and cause of hypertension.SBP is mainly concerned with kidney damage .[14]NIH detection and follow up programmed observed 12 deaths by renal failure among 7825 mild hypertensive patients with DBP 90 – 104 mmHg which constitutes 0.15 % and 13 deaths by renal failure among 3175 patients with DBP > 105 mmHg that is 0.42 % deaths are due to renal failure .[15]

Clinically microalbuminuria (a random urine Albumin Creatinine Ratio 30 -300 mg / g) or macroalbuminuria (a casual urine ACR more than three hundred mg / g) are the early markers of kidney damage. They are not only indicators of renal damage but also markers of progression of kidney damage .[16, 17-20]

Though obesity is a major risk factor for development of hypertension and CKD, less attention is paid to link between CKD and Obesity. Particularly visceral obesity / central obesity has strong link with CKD through two causes: hypertension and diabetes mellitus .[21]

Elevated blood pressure affects approximately one billion people that is one fourth of adult population worldwide and also major cause of death all over the world. Hypertension is one of the major cause of outpatient visit to a physician. So the

physicians have to identify and manage the obese individuals to prevent the complications and morbidity.

Reduction in the BP ,will slow down the rate of renal function decline in CKD.[13]Reduction in weight of only 5–10 percentage reduces the bloodpressure in normotensive in addition to obese individuals with elevated BP and need for the anti-hypertensive drugs are reduced.[9]

So to avoid all these complications of obesity particularly of central obesity, like hypertension and CKD, we must make awareness about physical fitness and importance of maintenance of normal body weight through regular physical activity and health education about healthy food habits .

This study was done to investigate the association of BMI and WC with hypertensive-CKD (stage I – II).

So by simple health education about healthy diet,physical activity,life style modification we can prevent excess body fat accumulation and related complications such as hypertension and kidney damage.

AIMS AND OBJECTIVES

AIM:

The aim of the present study was to evaluate the association of body mass index & waist circumference with hypertensive chronic kidney disease (stage I – II).

OBJECTIVE:

The purpose of this present study was to investigate whether waist circumference (WC) is more linked with GFR (renal function) reduction than body mass index (BMI) in patients with stage I – II hypertensive chronic kidney disease (CKD).

REVIEW OF LITERATURE

OBESITY :

Obesity is a chronic disorder with an increase in body weight and also an excess adipose tissue mass. A recent report by WHO stated that 1.6 billion people are overweight (BMI 25 to 30 Kilogram / meter^2), 400 million people are obese (BMI more than 30 Kg / m^2) worldwide.[22]

There are two major types of adipose tissues namely WAT (White adipose tissue) and BAT (Brown adipose tissue). Triglyceride (TG) storage is the major function of adipocyte.TG is mainly derived from chylomicrons (from diet) and VLDL from liver. Triglyceride is hydrolyzed by hormone sensitive lipase (HSL) to free fatty acid (FFA) into the circulation. There is continuous TG redistribution between adipose tissue and other parts of body. [2,23]

Excess fat is stored in the abdominal region (upper body fat) or in the gluteal-femoral region (lower body fat). Intra abdominal fat cells are smaller than fat cells in subcutaneous tissue and are more responsive to dietary and hormonal factors than those from other areas. Human adipose tissue is richly supplied by alpha and beta adrenergic receptors-beta agonists stimulate lipolysis and alpha-2 agonists inhibit lipolysis. Lipoprotein lipase (LPL) plays important role in controlling the regional distribution of fat.

Factors increase LPL activity :

1. Insulin
2. Cortisol.

Factors inhibit LPL activity :

1. Growth hormone

2. Catecholamines

3. Tumor Necrotizing Factor (TNF)

4. Cytokines

5. Testosterone.

Noradrenaline (α_2 & β) has more marked response in abdominal fat than gluteal and femoral tissues.Gluteal and femoral tissues contain large fat cells.

Body weight mainly depends on the steadiness between ingestion of calories and their utilization. When the caloric intake exceeds caloric utilization that will lead to Obesity.There is meal-to-meal regulation of food intake and also body weight is maintained at a given set point. Hypothalamus & some parts of brain play key role in the control of food intake. Hypothalamus has lateral "feeding center" in the median forebrain bundle and a medial "satiety center " in the ventromedian nucleus.[1,2,3,23]

Factors that influence appetite :[1, 2, 13 ,14, 23 ,24]

Increase food intake (Orexigenic):

- AGRP, β-endorphin, Galanin, Ghrelin, GHRH, MCH, Neuropeptide-Y, Orexin-A, Orexin-B

Decrease food intake (Anti-Orexigenic):

- Bombesin, CART, CCK, CRH, cGRP, Glucagon,GLP-1,2 GRP, Leptin, Neurotensin, Oxytocin, Peptide-YY, Somatostatin, α-MSH.

POMC is cleaved by PC-1 to give alpha MSH and this alpha MSH via MC4R which is present in the brain that regulates the intake of food and controls autonomic function and finally suppress the appetite and thereby food intake.

Ghrelin (288) is an aminoacetylated peptide which is secreted by Oxyntic cells of fundus of stomach. Concentration of Ghrelin is high before meals and reduced after ingestion of meals.

Ghrelin concentration is inversely related to BMI, while Insulin & leptin are directly related to BMI.

Neurotransmitters of CNS :

Appetite inhibitors : dopamine, serotonin, GABA

Appetite stimulators : opiods.

Endocannabinoid system is implicated in control of central food intake pathway and peripheral pathway of food ingestion and energy balance management.

Cannabinoid receptor 1 – present in cerebral cortex, cerebellum, hippocampus

Cannabinoid receptor 2 – present in the periphery.

MCH – is a polypeptide secreted by the fish pituitary and controls their skin colour,in mammals m RNA of MCH mainly found in lateral hypothalamus and zona incerta.

CART-neuropetide in hypothalamus inhibits food intake.

Other factors :

Cold weather,empty stomach-increased food intake.

Warm weather,distension of gastrointestinal tract-decreased food intake .

Obesity is an individual's response to the environment or otherwise results from interaction of ecological and heritable factors. So many genes are implicated in the origin of obesity such as genes controlling adipocyte differentiation, adipocyte specific adrenergic receptors, leptin production is controlled by 'ob' gene, 'db' gene that controls receptor for leptin and mutation of 'ob' gene or 'db' gene causes obesity, 'agouti' gene which is normally expressed in skin and regulates the melanin production, obesity results from mutation of Agouti gene, 'fat' gene and mutation of carboxypeptidase – E results in obesity.

Longterm effects of Leptin to elevate the bloodpressure are mostly mediated through the SNS which is again mediated by means of hypothalamic pro-opiomelanocartin. The chief connection between obesity and stimulation of SNS is POMC-MC4R pathway. Mutations in POMC or MC4R result in morbid obesity. Intact number and sensitivity of beta adrenoreceptors is required for the sympathetic signal transmission to the target tissues. β_3 Adrenergic receptor is associated with increased capacity to gain weight and higher WHR.RNA that encodes for β_3 adrenergic receptor is mainly expressed in intra-abdominal, visceral adipose tissue and in BAT but not in subcutaneous adipose tissues in humans.Reduced sympathetic

activity results in decreased thermogenesis and subsequent food intake stimulation and positive energy balance leading to obesity.

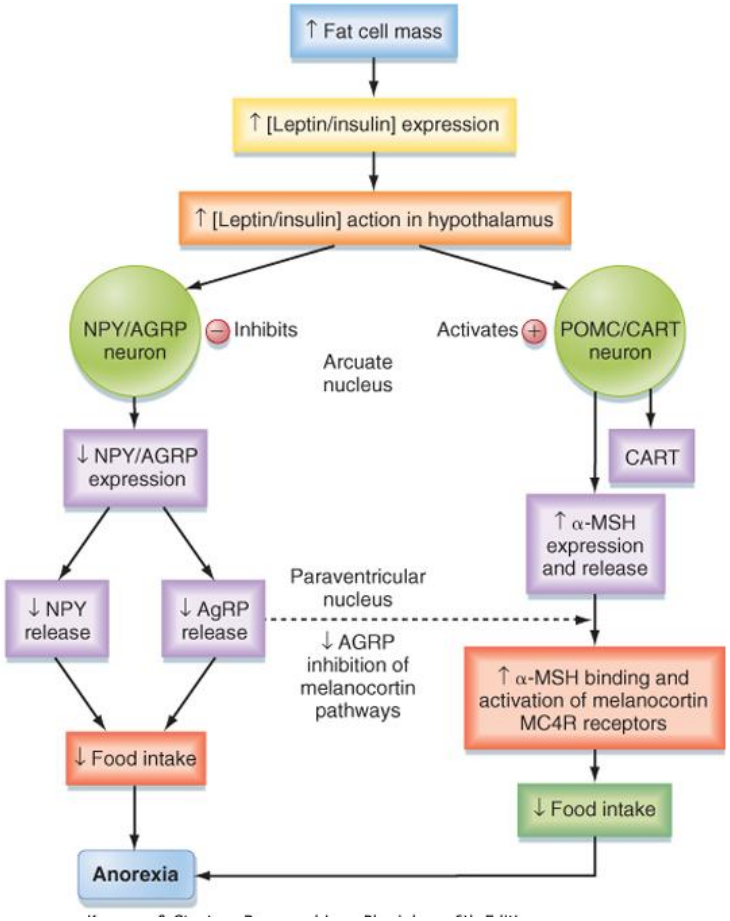

Figure-1.Effects of leptin in the brain.(Berne & Levy Physiology-6th edition)

Leptin(167aminoacids and16 Kd), ob gene product, is produced by the white adipose tissue and also by skeletal muscle, placenta, stomach. It's concentration in blood is proportional to the amount of fat depots.

Leptin receptors are present in hypothalamus-arcuate, dorsomedial, ventromedial and ventral premammilary nuclei and also present in extrahypothalamus sites-Nucleus Tractus Solitorius, the Substantia Nigra, theVentral Tegmental area.

In obesity the resistance to leptin is the major cause than lack of leptin. Leptin m RNA expression is amplified by fasting, hypothalamic damage and decreased by feeding.

Types of obesity phenotypes :[2]

1. Type one obesity-excess body fat/body mass
2. Type two obesity-excess subcutaneous truncal and abdominal fat(Android)
3. Type three obesity-high abdominal visceral fat
4. Type four obesity-excess gluteo femoral fat (gynoid)

Upper body obesity is a more significant cardiovascular hazard factor than BMI alone. Upper body fat accumulation is called as 'Android' type (apple shaped / abdominal / visceral / central / intra abdominal) obesity, and the lower body fat accumulation is called as 'Gynoid' type (generalized / pear shaped / subcutaneous fat) obesity.

Central obesity, which is measured by waist circumference (WC) and waist hip ratio(WHR), is a better interpreter than BMI to reflect visceral fat. WC was a strong predictor for both abdominal and non-abdominal fat.

Body Mass Index (BMI) also known as Quetelet Number / Quetelet Index is derived by a formula ,[2,3,23]

BMI (Kg / m^2) = Weight in Kilograms / Height in $meter^2$

Weight in lbs / Height in $inches^2 \times 703$ calculates the BMI.

Body adiposity classification based on BMI – NIH and WHO :[2,3,13,14,23]

CATEGORY	BMI (Kg/M^2)	OBESITY CLASS
Under weight	Less than 18.5	
Normal weight	18.5 to 24.9	
Over weight	25.0 to 29.9	
Obesity	30.0 to 34.9 35.0 to 39.9	I II
Extreme Obesity	More than or equal to 40.0	III

NIH –National Institutes of Health,

Ethnic specific values for Waist Circumference (WC) :[25]

ETHNIC GROUP		WAIST CIRCUMFERENCE
EUROPEANS	MALE	≥ 94 cm(37 inches)
	FEMALE	≥ 80 cm(31.5 inches)
SOUTH ASIANS & CHINESE	MALE	≥ 90 cm(35 inches)
	FEMALE	≥ 80 cm(31.5 inches)
JAPANESE	MALE	≥ 85 cm(33.5 inches)
	FEMALE	≥ 90 cm(35 inches)

BMI provides an estimate body fat .Low level of BMI thresholds for overweight and obesity have been proposed for Asians especially China and India.

Assessment of body fat and its distribution:

- Height & Weight
- Circumferences
- Density-Immersion and Plethysmograph
- Skinfolds
- Ultrasonogram
- Heavy water
- Fat soluble gas
- Total body electrical conductivity
- Absorptiometry (DEXA-dual energy x-ray absorptiometry)
- Computed tomography (CT)
- Magnetic Resonant Imaging (MRI)
- Neutron activation

  Elevated WC and elevated BMI may precede the onset of morbidity and mortality.

For some obesity complications, the regional distribution of fat rather than the absolute excess adipose tissue amount appears to be important .Abdominal obesity is closely associated with type -2 DM, metabolic syndrome, cardiovascular diseases ,kidney damage etc.[2,313,23)]

Complications of obesity :[(2, 3, 13, 14 , 22, 23 ,26)]

Psychosomatic, Osteoarthritis of knee joints an& hip joints,Varicosity of long veins, Hiatus hernia,gall bladder stones,Postoperative problems, sprain in back, Accident

proneness, Obstructive sleep apnoea, Hypertension, Breathlessness, myocardial infarction, Stroke,Type-2 diabetes mellitus, high lipid level in blood, irregular menstrual cycle, raised carcinoma risk, Heart failure.

Excess accumulation of abdominal or visceral adipose tissue is associated with high apo-lipoprotein B concentration and reduced plasma HDL level.

Individuals with excess visceral adipose tissue have high glycemic response to glucose challenge in the presence of hyperinsulinemia which indicates insulin resistance.

Metabolic changes connected with excess visceral adipose tissue (resistance to insulin, glucose intolerance, high level of insulin in blood) are considered as risk factors for Non Insulindependent Diabetes Mellitus, metabolic syndrome / syndrome X , cardiovascular diseases.

Insulin resistance is selective (mostly involving metabolism of glucose), tissue specific (mainly affects skeletal muscle), and pathway specific (glycogen synthesis is mostly affected) in obese hypertensive individuals. And this may modulate the hypertension development through various mechanisms such as enhancement of renal sodium retention, R-A-A-S activation, sympathetic nervous system activation etc….

Obesity treatment :[2, 3, 22, 23]

1. Diet
2. Exercise
3. Behavior therapy

4. Pharmacotherapy
5. Surgery

Pharmacotherapy:

Orlistat :

It is a derivative of lipostatin. It inhibits gastric lipase and pancreatic lipase. So that reduces fat absorption and increases triglyceride (TG) excretion in stools.

Sibutramine :

It inhibits serotonin (5-HT) and norepinephrine (NE) reuptake at nerve endings.

Surgical management of obesity :

1. Surgeries that cause malabsorption :
    - Roux – en – Y gastric bypass surgery
    - Biliopancreatic diversion
2. Surgeries that cause gastric restriction :
    - Vertical banded gastroplasticity
    - Laproscopic adjustable gastric banding.

HYPERTENSION :

Raised blood pressure is one of the major public health issues in developed countries.A variety of systems are concerned in the control of arterial blood pressure including peripheral and / or central adrenergic system, renal system , hormonal and vascular systems. Overweight and obesity are key risk factors for

primary / essential hypertension which accounts for 65 – 75 percentage of the hazard for essential hypertension.[5]Obesity is coupled with Hypertension(HT), Proteins in urine, progressive kidney disease.

Ohnishi et al[27] in their study observed that abdominal obesity was correlated with high incidence of hypertension ,**Albert et al**[28],in their study they induced weight gain in dogs and suggested that increase in weight was associated with increase in heart rate, BP, cardiac output, plasma volume and fasting insulin concentration.

Various other studies suggested prolonged high fat diet induced weight gain,increased the bloodpressure.[29-31]Various studies reported BP is associated with obesity indices BMI,WC,WHR .[5,8]And some other studies showed weight gain is a good interpreter of hypertension .[4,6,7] Weight loss is effective in the prevention of elevated bloodpressure .[2,3,13,14,22,32-36] Even 5–10 % weight loss reduces the bloodpressure in normotensive as well as in hypertensive obese individuals. Hypertension is one of the most major reason for renal, cardiovascular and cerebrovascular harm.

AGE	**BLOOD PRESSURE(mmHg)**
AT BIRTH	60 – 75 / 40
CHILDHOOD	90 – 100 / 50
PUBERTY	100 – 120 / 60
ADULT	120 – 140 / 80
≥ 60 YEARS	140 – 160 / 80 – 90

Blood pressure changes with age.

Classification of blood pressure for adults > 18 yrs old :[13,25,32-36]

(**2003 European Society of Hypertension - European Society of Cardiology Guidelines for the management of Hypertension)**

CATEGORY	**SBP (mmHg)**	**DBP (mmHg)**
Optimal	Less than 120	Less than 80
Normal	Less than 130	Less than 85
High normal	130 to 139	85 to 89
HT-stage 1(mild)	140 to 159	90 to 99
HT-stage 2 (moderate)	160 to 179	100 to 109
HT-stage 3 (severe)	More than 180	More than 110
Isolated systemic HT	More than 140	Less than 90

Two major types of hypertension are :

1. Essential / idiopathic / primary hypertension –arterial hypertension with no definable cause.It accounts for > 90 % of all hypertension cases.

2. Secondary hypertension – specific structural organ or gene defect is responsible for hypertension. It may be due to renal cause, endocrine cause or due to diverse causes.

Overweight and obesity are the key risk factors for primary/ essential hypertension.Visceral fat accumulation--→ Insulin resistance and adipokines disorders --→ increase reabsorption of sodium by the kidney, overactivity of

sympathetic nervous system, vascular smooth muscle proliferation, atherosclerosis --→hypertension.[2,3,16,20]

Augmented sodium reabsorption from the renal tubules and loss of pressure natriuresis play significant part in initiating hypertension associated with weight gain.

Mechanisms involved are:

1. Increased sympathetic nervous system function
2. Stimulation of Renin-Angiotensin-Aldosterone-System
3. Kidney is compressed physicaly by the fat deposition within and around the kidney.

Augmented adrenergic activity plays major role in the development and continuation of obesity hypertension in experimental animals and in humans. The renal sympathetic nerve mediates most of the longterm effects of sympathetic nervous system (SNS) stimulation on blood pressure in obesity.

Mediators of SNS activation in obesity:

- Hyperinsulinemia
- Angiotensin II
- ↑ed level of FFA
- Baroreceptor reflexes impairement
- Activation of chemoreceptor mediated reflexes coupled with sleep apnoea
- Cytokines released by the adipocytes(adipokines) are Leptin,TNF-α,IL-6.

Hypertension is the major cause for renal, cardiovascular and cerebrovascular impairment.

Effects of hypertension on various organs .[13, 14, 33-36]

1. On the Heart :

Concentric left ventricular hypertrophy which ultimately dilates the cavities and leads to heart failure.

2. Neurological effects :

-Hypertensive retinal changes

-Occipital headache particularly in the morning is one of the prominent early symptom of Hypertension.

-Cerebral ischemia

- Cerebral haemorrhage

- Hypertensive encephalopathy

3. On the Kidney :

Arteriosclerotic lesions of the afferent arteriole and efferent arteriole and the glomerular capillary tufts are leading to reduction in GFR and also to tubular dysfunction. Approximately 10 % of the deaths by Hypertension results from renal failure.

In chronic sustained hypertension, stretch activated ionic channels are activated and also there is early gene response. Cytokines like TGF-β, growth factors like angiotensin-II, EGF, PDGF, CTGF lead to myointimal proliferation and sclerosis finally cause vasoconstriction and sclerosis.

In malignant hypertension, haemodynamic stress causes massive fibrinoid necrosis of afferent arteriole and glomeruli, thrombotic microangiopathy, a nephritic urinary sediment and acute renal failure.

HYPERTENSIVE CHRONIC KIDNEY DISEASE :

The kidney be a target and also a root of hypertension. When there is increase in the arterial pressure, renal arterial pressure enhances the excretion of sodium and water until the arterial pressure returns to normal value. Kidneys play major role in long term control of blood pressure .[1,24]

Filtering the plasma and removing the substances from the filtrate at variable rates is the important function of the kidneys.

Nephron is the key structural and functional unit of the renal system. Each kidney consists of about 80,000 to 1,00,000 nephrons.

Each nephron contains 1.Glomerulus – is a modified capillary network that delivers an ultra filtrate of plasma to Bowman's space 2.Tubule – here the filtrate is converted into urine.

The main physiological components of renal functions are:

1. GFR, 2. RBF, 3. Glomerular permeability.

The first step in urine formation is glomerular filtration (GF). Plasma is ultrafiltrated by glomerulus to get the GF. In normal adult male the glomerular filtration rate (GFR) ranges from 90 – 140 ml / min and in female it ranges from 80 – 125 ml / min.[39]Thus in 24 hours,glomeruli filtered as much as 180 L of plasma. This GF is devoid of cellular elements and devoid of protein .[39]

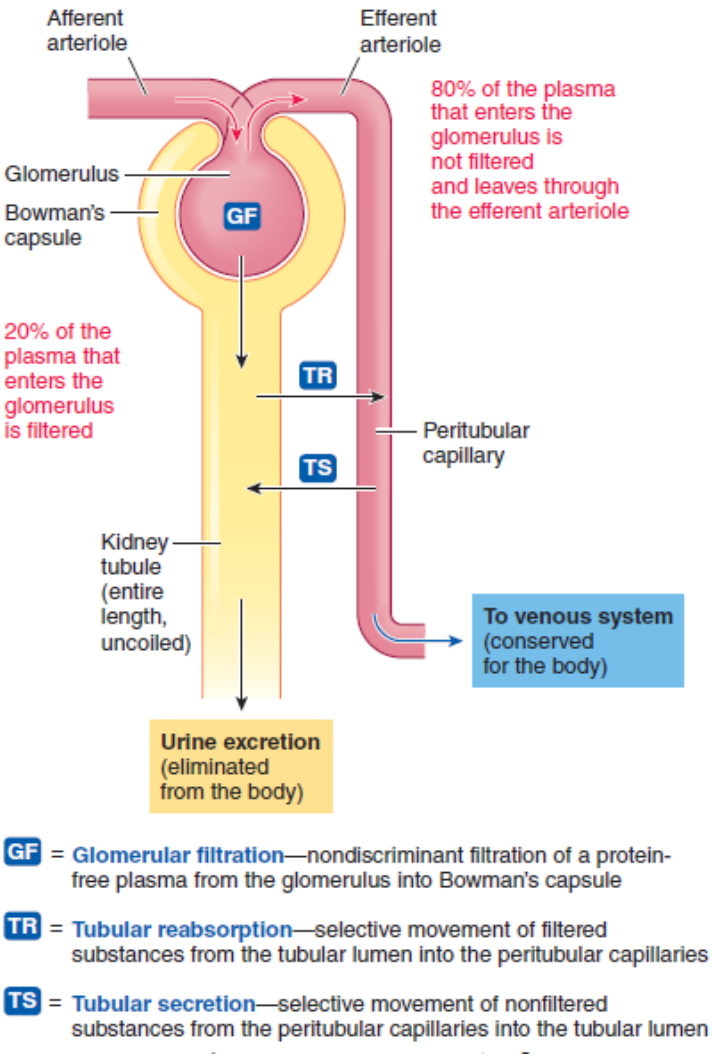

Figure -2. Basic renal processes .(Sherwood Human Physiolgy-4th edition.)

$$GFR = K_f [(P_{GC} - P_T) – (\pi_{GC} – \pi_T)]$$

K_f =Glomerular ultrafiltration co-efficient

P_{GC}=Glomerular hydrostatic pressures

P_T =Mean tubular hydrostatic pressure

π_{GC}=Glomerular capillary plasma osmotic pressure

π_T =Tubular filtrate osmotic pressure

GFR depends on Glomerular blood flow,Ultra filtration pressure, the area and the composition of the filtration barrier.

The net filtration pressure (P_{UF}) is 15 mmHg at the afferent arteriolar end and falls to zero at the efferent end of glomerular capillary.[1]

Factors affecting the GFR :[1,16,17,20,24,39,40]

- Alteration in blood flow to the kidney (RBF)
- Alteration in Glomerular capillary hydrostatic pressure
- Systemic hypertension
- Afferent and efferent arteriolar narrowing
- Plasma proteins concentration change (dehydration, hypoproteinemia)
- Edema of kidney inside tight renal capsule
- Changes in Bowman's capsule hydrostatic pressure
- Ureteral obstruction
- Any alteration in filtration co-efficient
- Changes in Glomerular capillary permeability
- Changes in Effective filtration surface area.

The GFR can be measured by various methods :[1, 24, 40]

- Inulin clearance test

  C_{INULIN} (or GFR) = U_{in} V / P_{in} = 35 × 0.9/0.25

  =126 ml / min.

- Creatinine clearance test

  C = UV / P

The plasma creatinine concentration is inversely proportional to GFR.

- Urea clearance test

  Urea clearance is less than the glomerular filtration and also protein diet influences GFR. So it is not as sensitive as the previous one to assess the renal function.

K_f is altered by mesangial cells.mesangial cell contraction producing a decrease in K_f

Factors causing mesangial contraction and relaxation:

Relaxation :

Atrial natriuretic peptide (ANP), Dopamine, Prostaglandin E_2 , c AMP

Contraction :

Endothelins, A-II, Vasopressin, Norepinephrine, Platelet activating factor (PAF), PDGF, Tx - A_2, Prostaglandin F_2, Leukotreins-C_4 and D_4, Histamine

PHYSICAL DETERMINANTS	**PHYSIOLOGIC / PATHOLOGIC CAUSES**
$\downarrow K_f \rightarrow \downarrow$ GFR	Renal diseases, diabetes mellitus , high bloodpressure
$\uparrow P_{BC} \rightarrow \downarrow$ GFR	Urinary tract obstruction (eg.nephrolithiasis)
$\uparrow \pi_{GC} \rightarrow \downarrow$ GFR	↓ bloodflow to kidney , ↑ plasma proteins
$\downarrow P_{GC} \rightarrow \downarrow$ GFR	Reduced arterial pressure
$\downarrow R_E \rightarrow \downarrow P_{GC}$	Decreased Angiotensin – II
$\uparrow R_A \rightarrow \downarrow P_{GC}$	Increased Sympathetic activity , vasoconstrictor hormones (norepinephrine,endothelins)

HORMONES / AUTOCOIDS	**EFFECT ON GFR**
Norepinephrine	Reduced
Epinephrine	Decreased
Endothelin	Reduced
Angiotensin – II	↔
Endothelin derived Nitric Oxide	Elevated
Prostaglandin	Raised

Intrinsic feedback mechanism in kidneys normally keeps the renal blood flow (RBF) and GFR relatively constant. The relative constancy of GFR and RBF is called Autoregulation.GFR and RBF are also substantially controlled by SNS, catecholamines, angiotensin-II, prostaglandins, nitric oxide, endothelin, natriuretic peptdides, bradykinin and adenosine.

Renal blood vessels which includes afferent and efferent arterioles are richly supplied by sympathetic nerves. Strong activation of sympathetic nerves causes constriction of renal arterioles leading to decrease in the RBF and GFR.

Macula densa feedback mechanism for autoregulation of P_{GC} and GFR consists of afferent arteriolar feedback mechanism and efferent arteriolar feedback mechanism. This feedback mechanism depends on JGA (Juxta Glomerular Apparatus).

JGA includes :

1. Macula Densa cells –specialized epithelial cells of distal tubule of kidney.

2. JG cells – present in the afferent and efferent arterioles.

3. Mesangial cells

Elevated blood pressure causes failure of autoregulation of afferent arteriole bloodflow, this causes glomerular hypertension which leads to hyperfiltration, hypertrophy and focal segmental glomerulosclerosis which again causes loss of autoregulation. [16,20,24,41]

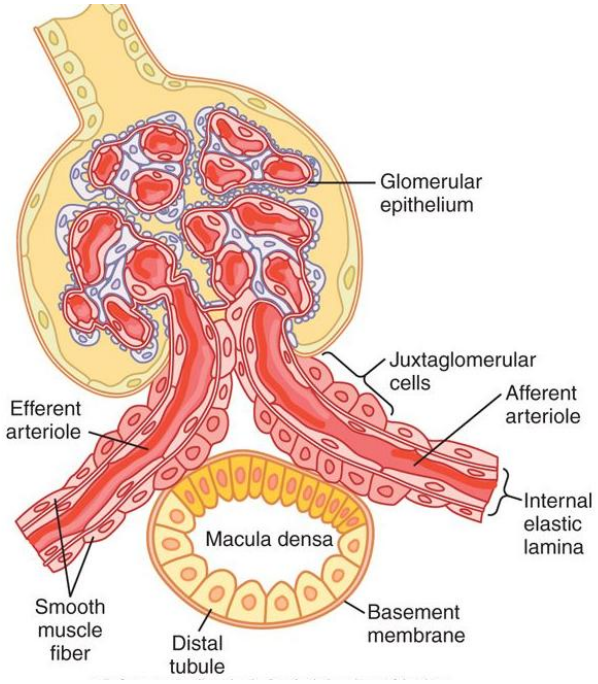

Figure-3.Structure of JGA.(Guyton and Hall-Textbook of Medical Physiology-12th edition).

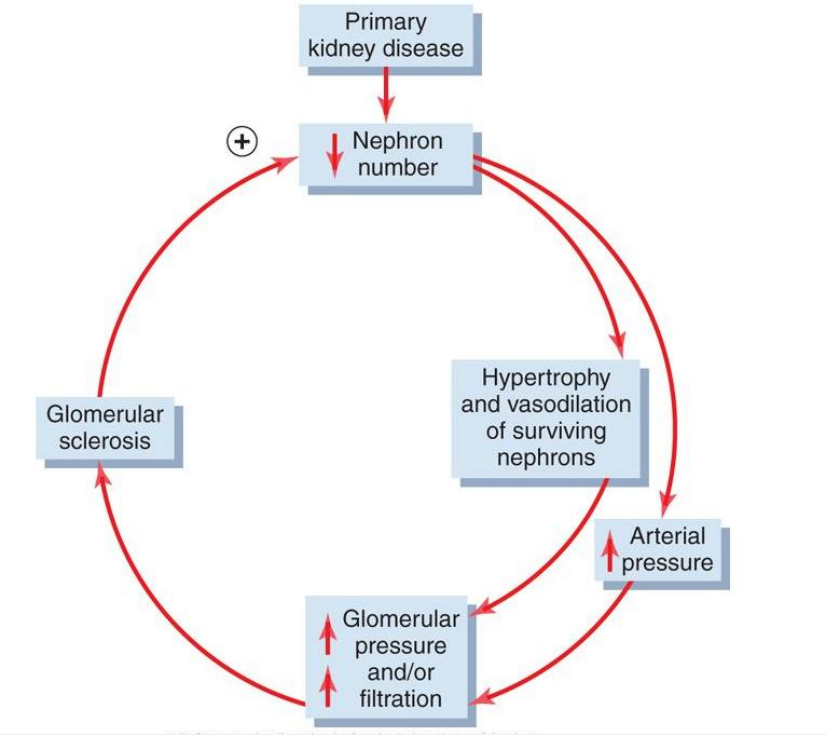

Figure-4.Viscious circle that can occur with primary kidney damage. (Guyton and Hall-Textbook of Medical Physiology-12th editon).

The risk associated with hypertension is graded and continuous. The risk for renal injury is strongly related to systolic blood pressure (SBP) more than diastolic blood pressure(DBP).

Among chronic renal disease patients in the Modification of Diet in Renal Disease (MDRD) study, greater baseline MAP (mean arterial pressure) measurements were independently prognostic of a greater rate of GFR reduction.[43]The magnitude of increased risk of ESRD is associated with the blood pressure level, so even mild elevations of blood pressure lower than the threshold level for diagnosis of hypertension were associated with increased ESRD risk.

Another study said that although elevated blood pressure is an independent risk of ESRD systemic hypertension is associated with increased risk of ESRD .[43]

The degree of arcuate and interlobular arterial thickening is related to the severity of

hypertension. There are two patterns of hypertensive glomerulosclerosis .[37, 38]

1. Ischaemic obsolescence – collapsed glomerular tufts surrounded by intercapsular fibrosis filling the Bowman's space.

2.Glomerular solidification – global glomerulosclerosis seen.Loss of glomerular tuft cells and collagen and matrix material deposition in the Bowman's space,fragmentation of Bowman's capsule and the solidified tuft merges with the surrounding ineterstitial fibrous tissues. Obesity induced kidney damage is due to many factors like hormones, pro-inflammatory

molecules produced by adipocytes, high level of mineralocorticoids, reduced adiponectin levels.[14,16,20,41]

Chronic Kidney Disease (CKD) is a pathologic process with multiple etiologies, resulting in the inexorable attrition of number of and function of nephron and frequently leading to ESRD.

NKF-KD provides CKD definition as:[45]

1 .Kidney injury for more than three months, as defined by structural or functional renal abnormalities, with or without reduction in GFR, manifested either :

- abnormal pathological lesions or
- markers of renal injury, with abnormalities in the blood or urine composition or abnormal imaging test.

2. GFR less than 60 ml / min / 1.73 m^2 for more than three months, with or without kidney damage.

Incidence of CKD, progression of CKD and the incidence of ESRD are increased with elevated systolic blood pressure.

Albuminuria is one of the oldest and most sensitive marker of the kidney damage.[16,17,20,44]

Protienuria can also be measured by various methods.

- Radio immuno Assay-using double antibody technique;
- Immunoturbidimetric method,
- Laser nephelometer;

- ELISA ;
- High performance liquid chromatography.

Prevalence of CKD (% of the population affected)[26] :

CKD STAGES	AGE (YEARS)			
	Under 65 (%)	**65 to 74 (%)**	**75 to 84 (%)**	**More than 85 (%)**
III	1.4	15.4	29.4	30.9
IV	0.04	0.4	1.3	2.4
V	0.03	0.1	0.2	0.1
Total	1.5	15.9	30.9	33.4

Categorization of CKD into 5 stages is mainly to manage the patients according to the stages.

Risk factors of CKD:(13,14,16,17,20,42)

-Inherited renal disease in family, Elevated bloodpressure, Diabetes Mellitus, Autoimmune disease, Older age, Past episode of ARF

The following table shows the incidence of risk factors causing CKD :

The percentage of hypertension causing CKD is 27.4 %, the elevated blood pressure is the second common cause of CKD, next to diabetes mellitus.

PRIMARY CAUSE	INCIDENCE (%)
Diabetes mellitus	44.8
Hypertension,Large vessel disease	27.4
Glomerulonephrtis	7.7
Interstital nephritis	3.4
Cystic,Heriditary,Congenital disorders	3.1
Neoplasms,Tumours	2.4
Secondary glomerulonephritis,Vasculitis	2.2
Cause unknown	7.5

Functions of kidney and renal function impairment in CKD patients:[17]

KIDNEY FUNCTION	CONSEQUENCES OF DYSFUNCTION
Maintainance of concentration & body electrolyte and fluid volume control	Reduced plasma sodium level, low plasma potassium, Hypocalcemia, high phosphate in blood
Controls blood pressure	Hypertension, diseases of Cardiovascular system
Mediator of Endocrine function	Anaemia,Hypertension,Bone disease,Low vit-D activation,Prolonged half-lives of peptide hormones
Removal of Waste products	Anorexia,Nausea,deposition of oxalates and phosphates in Soft tissue,Neurologic dysfunction, muscle protein loss.

Classification and staging of Chronic Kidney Disease(CKD) by the National Kidney Foundation: [16,17,20,41]

STAGE	DESCRIPTION	GFR(ml/min/1.73m^2)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mild reduction in GFR	60 to 89
3	Kidney damage with moderate decrease in GFR	30 to 59
4	Kidney damage with severe ↓ GFR	15 to 29
5	Renal failure	Less than 15 or dialysis

Kidney damage - pathological abnormalities / abnormality in blood or urine investigations or imaging studies.

Stage 3 to 5 CKD patients are vulnerable to fluid accumulation, volume overload, high plasma potassium, hyponatremia and azotemia. Once GFR has decreased below a critical level, CKD tends to develop to ESRD regardless of initial injury.

Hypertension especially systolic hypertension is a powerful promoter of renal injury. Bloodpressure control reduces the threat of CKD progression.

Risk factors for progression of kidney disease: [46]

- Proteinuria more than 1.5 g / 24 hour or urine protein to creatinine ratio more than 1 g / g.

- Elevated bloodpressure
- Type of underlying renal pathology
- African American race
- Males
- Obesity and dyslipidemia
- Smoking
- High protein diet
- Phosphate retention
- Metabolic acidosis

Complications of Chronic Kidney Disease(CKD): [13,14,42]

All organs are affected, but important complications are ;

Anaemia, Loss of energy, Decreasing appetite, nutritional status disorder, Abnormalities in calcium and phosphorous metabolism accompanied by metabolic bone disease, Abnormalities in sodium, water, K^+ and acid-base homeostasis.

Management of CKD :

Stage 1-2 : Diet adjustment,management of BP and glycemia, R-A-A-S inhibitors

Stage 3 : management of anaemia, renal bone disease , dietary modification

Stage 4 : 3 + haemodialysis(if needed) and End Stage Renal Disease management

Stage 5 : 4 + dialysis + CKD complication management.

So according to stages CKD is managed.

By assessing the clinical presentation we can presume the etiology: [14]

CAUSE	CLINICAL PRESENTATION
Diabetic kidney disease	Diabetes,Proteinuria,Retinopathy
Hypertension	Elevated blood pressure,normal urine analysis,family history
Non diabetic glomerular disease	Nephritic or nephritic presentation
Cystic renal disease	Renal tract symptoms, abnormal sediments in urine,abnormal radiologic imaging tests.
Tubulointerstitial disease	Urinary tract infection and reflux,longterm medication,abnormal urine analysis,abnormal urinary imaging.

Laboratory investigations in renal insufficiency: [47]

URINE :

Simple urine analysis is important to diagnose renal damage esp. chronic kidney disease.

- Dipstix examination
- Urine examination (RBC, RBC casts, WBC, WBC casts, Tubular cells, Granular casts, Oval fat bodies, Fatty casts or Free fat)
- Quantitative analysis of twenty four hour urine volume

BLOOD :

- Complete blood count (CBC)
- Autoanalyser profile (blood urea, serum creatinine, bicarbonate, calcium, phosphate, alkaline phosphatase, glucose, Hb $A1_C$)
- Serological tests (HBsAg, HBsAb, HCAb, HIV, ANF, ANCA, Anti-GBM, Anti-ds-DNA)

RADIOLOGICAL INVESTIGATIONS :

- X-ray chest (CXR)
- Renal ultrasonogram
- Renal tract plain radiograph
- IV urogram, CT scan, MRI, renogram, angiogram.

ECHOCARDIOGRAM

ECG

RENAL BIOPSY

Comprehensive strategy for renoprotection in CKD patients : [32]

1. ACE Inhibitors – ARB
2. Antihypertensive management
3. Nutritional protein restriction
4. Strict glycemic control
5. Cessation of smoking
6. Lipid lowering treatment

Protein composition of normal urine : [46]

In healthy adults, minimal amount of glomerular and tubular origin proteins are excreted, averaging 80 mg / 24 hours.

PROTEIN	EXCRETION(mg/day)
Plasma protein	
1. Albumin	12.0
2. Ig G	3
3. Ig A	1
4. Ig M	0.3
5. Light chains	
• κ	2.3
• λ	1.4
6.β microglobulin	0.12
7.other plasma proteins	20.0
Total plasma protein	40.0
Non plasma protein	
1. Tamm-Horsfall protein	40.0
2. Other non renal derived protein	< 1
Total non plasma protein	40.0

Total urinary protein = 80 ± 24 (SD) mg / day.

Microalbuminuria: [44-47]

The main markers used to assess renal function damage are GFR, microalbuminuria and macroalbuminuria. The chief determinants of microalbuminuia are central or abdominal obesity and systolic blood pressure. Microalbuminuria is defined as 30 – 300 mg albumin / 24 hr urine. Albuminuria is defined as (more than 300mg/24 hrs) a persistent excretion rate exceeding that of microalbuminuria. Microalbuminuria and macroalbuminuria were independent ESRD predictors after 10.3 years.

Most plentiful plasma protein is albumin. Urinary excretion of albumin is determined by the combined effects of glomerular filtration and processing by renal tubules.

Albumin concentration in glomerular ultrafiltration is between 1 and 50 μg/ ml, this corresponds to albumin filtration load between 170 mg and 9 g per 24 hours, in healthy adults. [16]

Reduced GFR and albuminuria in combination were important predictors of ESRD.

Microalbuminuria is the earliest sign of nephropathy before it manifests as overt proteinuria.

Microalbuminuria is classified as:

1. Albumin Excretion Ratio (AER) : 20 to 200 μg / minute or 30 to 300 mg / day.
2. Albumin / Creatinine Ratio (ACR) : 2.5 to 25 mg / mmol.
3. Albumin / Creatinine : 30 to 300 mg / day.
4. Albumin Concentration (in early morning urine) : 30 to 300 mg / L.

Microalbuminuria denotes high probability of damage of the renal glomerular filtration capacity and is of great diagnostic relevance.

- In Diabetes Mellitus – for eary diagnosis of nephropathy.
- In Hypertension – ESRD indicator.
- MA is also associated with cardiovascular diseases.

Interfering factors of microalbuminuria estimation :

- Sternous exercise
- High protein diet
- High salt intake
- Haematuria
- Menses

Microalbuminuria is associated with :

- Diabetic Mellitus with early diabetic nephropathy
- Hypertensive cardiovascular diseases
- Generalized vascular diseases
- Pre-eclampsia

Microalbuminuria also occurs in :

- Ischemia
- Trauma
- Thermal injury
- Surgery

- Pancreatitis
- Inflammatory bowel disease (IBD)

GFR estimation equations (e GFR) : [16,20,41-47]

The GFR level can be estimated by using formula which includes serum creatinine level and some variables for instance age, gender, body size and race.

Modification of Diet in Renal Disease (MDRD) equation :

$$GFR\ (ml/min) = 170 \times [\text{ serum creatinine level(mg/dl) }]^{-0.999} \times [\text{Age (years) }]^{-0.176} \times (\text{ 0.762,if female }) \times (1.180 \text{ if African American race}) \times (\text{ BUN mg/dl })^{-0.170} \times (\text{Albumin })^{0.318}.$$

Since the publication of NKF-CKD guidelines, the widespread method used to measure the renal function is the simplified four variable Modification of Diet in Renal Disease (MDRD) equation :

$$GFR\ (ml/min/1.73m^2) = 186 \times [\text{Serum Creatinine }]^{-1.154} \times [\text{Age in years}]^{-0.203} \times [0.742 \text{ if patient is female gender }] \times [1.212 \text{ if the patient is black race }].$$

CKD-EPI. Equation :

$$GFR\ (ml/min/1.73\ m^2) = 141 \times \min.(\text{serum creatinine} / K,^{1})^{\alpha} \times \max.(\text{serum creatinine} / K,^{1})^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ (if female)} \times 1.159 \text{ (if black)}.$$

K = 0.7 for female and 0.9 for male ;

α = -0.329 for female and -0.411 for male.

Cockcroft- Gauti Formula :

Creatinine clearance (ml/min) = [(140 – Age in years) × (Body weight in Kg)] / (Serum creatinine (mg/dl) × 72) ;

If the patient is female , this value is multiplied by 0.85.

Other formulas to measure GFR [48] :

Scwartz Formula :

GFR = 0.55 × Height (in cm) / Serum creatinine (mg / dl)

Counahan – Barrett formula :

GFR = 40 × Height (in cm) / serum creatinine (μmol / L)

Modified Schwartz formula :

GFR = 39.1 [Height (meter) / Serum creatinine level(mg / dl)] $^{0.516}$ × [1.8 / cystatin (mg / dl)] $^{0.294}$ × [30 / Blood Urea Nitrogen (mg / dl)] $^{0.169}$ [1.099] ^{male} [Height (in meters) / .4] $^{0.188}$

Creatinine: [25,44,47]

Serum creatinine is widely used to estimate GFR. Creatinine (MW 113 Da) is the cyclic anhydride of creatine which is produced by phosphocreatine decomposition. Creatinine is synthesized from methionine, glycine and arginine. Creatinine is excreted by the kidney. The rate of excretion of creatinine is constant relatively from day to day. Plasma creatinine and renal creatinine clearance are diagnostic indicators of renal function. Narrow range of serum creatinine level is mainly maintained by

glomerular filtration. The serum creatinine level initially changes slightly with decrease in the GFR. So minimal changes in the serum creatinine level will evoke major changes in the GFR level. But when the GFR decreases to < 40ml / min / 1.73 m^2, huge change in serum creatinine level correspond to little GFR changes occur.

Serum creatinine is estimated by two methods:

1. Chemical method,
2. Enzymatic method.

The Jaffe reaction (chemical method) : Creatinine reacts with picrate in alkaline medium which yields an orange-red complex.

Factors that affect serum creatinine level are :

- changes in the muscle mass,
- nutritional status,
- physical activity
- Metabolism of creatinine in gut.
- Drugs like diuretics, chloralhydrate, marijuana, guanethedine, furosemide, chloremphenical, sulfonamides.

Increased Creatinine level seen in the conditions such as :

- ❖ renal dysfunction,
- ❖ diminished renal blood flow (Shock , Dehydration),
- ❖ congestive heart failure,
- ❖ diabetes Mellitus (DM)

- ❖ Acromegaly, Gigantism
- ❖ Hypothyroidism

Decreased Creatinine level seen in :

- ➢ Muscular Dystrophy
- ➢ Polymyositis and neurogenic atrophy
- ➢ Hyperthyroidism
- ➢ Anaemia
- ➢ Inflammatory muscular diseases
- ➢ Advanced renal diseases and renal stenosis
- ➢ leukemia

Urea: [25,41-47]

Urea is a byproduct of the protein and aminoacid metabolism.Urea is mainly (90%) excreted by the kidney.

Factors that affect blood urea concentration are:

1. High protein diet,
2. Elevated protein catabolism,
3. Following GIT haemorrhage increased reabsorption of blood protein,
4. Cortisol treatment,
5. Dehydration,
6. Decreased renal blood flow.

Blood urea level can be estimated by two methods:

1. Chemical method,

2. Enzymatic method.

Enzymatic method is of four types:

1. Equilibrium photometric,
2. **Kinetic photometric,**
3. Conductiometry,
4. Dry chemistry system.

In **enzymatic method**, urea is first hydrolyzed by using urease to get ammonia .And this ammonia is quantified.

Other studies related to this present study :

Hyunju oh et al : [49] In their study "Waist Circumference(WC), not BMI ,is associated with renal function decline in Korean population : Hallym Aging Study ",454 persons with GFR > 60 ml/min/1.73 m^2 participated and followed for 6 years and their renal function decline was assessed. Their result showed that abdominal obesity and not Body Mass Index was correlated with faster renal function drop and so it may be a better interpreter than BMI for renal function decline.

Janssen et al: [50] studied about " WC and not BMI explains obesity related health risk ".It was a six years study included 14,924 persons aged more than 17years.WC,height,weight, serum cholesterol, Triglycerides, lipoprotein,glucose were

estimated.In their study they observed BMI together with WC does not predict an increased obesity related health problem better than WC alone.

In their study "Obesity ,anthropometric measures and CKD complications ", **Navaneethan et al** [51] included 2,853 adult CKD patients and WC, HC, BMI, Haemoglobin, total cholesterol, serum albumin and bicarbonate level ,PTH level,e GFR were measured .The result was ,Obese based on both WC and BMI had higher odds of CKD complications than non-Obese participants and those with BMI less than 30 Kg / m^2 with heigh WC was not associated with an with high WC was not associated with any CKD complications.

" Relationship between Abdominal Obesity (AO) and Microalbuminuria (MA) in elderly " was studied by **Mohmoud AH and Taha HM .** [52]This cross-sectional study included 200 elderly persons with the age group of > 60 years and Height,Weight,BMI,WC,HC,WHR were measured.Blood pressure was assessed and urine ACR was done.Statistical analysis was done by using independent t-test and paired-t-test.Conclusion was AO is strongly associated with Microalbuminuria in Egyptian elderly.

Ohnishi et al : [27]In their study about " Incidence of hypertension in individuals with abdominal obesity in a rural Japanese population : The Tanno and Sobetsu study ",396 individuals aged ≥ 30 years were participated .WC,BMI,Systolic blood pressure (SBP),Diastolic blood pressure (DBP),fasting plasma glucose,total cholesterol,TG,HDL were measured for all the participants.The unpaired t-test and χ^2 were used for statistical analysis.Group -1 included individuals with Abdominal

Obesity(AO) and Group-2 included non-AO .The result showed increased incidence of hypertension in group-1.

Seok Huikang et al : [53] studied " Association of visceral fat area (VFA) with CKD and Metabolic syndrome (MS) risk in the general population:Analysis using multi-frequency bioimpedence ".In this study,22,480 patients were grouped into low , middle , high tertiles based on their VFA.WHR,BMI,SBP,DBP,FPG,T.CH.,TG,AST,ALT and uric acid levels were increased as the VFA tertile increased and HDL level ,e GFR decreased as the VFA tertile increased.

"prevalence of Renal Insufficiency (RI) in individuals with hypertension and obesity / overweight : the FATH study " conducted by **Pablo Gomez et al** [54] in 5,585 pateints with hypertension and GFR $\geq$ 25 Kg / m^2.FPG,HbA_{1c} ,total cholesterol,LDL,HDL,TG,serum creatinine were analysed.e GFR was estimated by using MDRD and C – G equation.They observed that the occurrence of renal injury was greater in patients with abdominal obesity.

Kosaku Nitta [55] in his review article,he emphasised that 'metabolic syndrome which includes visceral obesity, dyslipidemia, hypertension, impaired insulin sensitivity was an important risk factor CKD and cardiovascular diseases.

Ribstein et al : [56] studied " Combined renal effects of overweight and hypertension " .In this comparative study,in hypertensive patients obesity causes a greater filtration fraction and more microalbuminuria, that showed that the increase in weight intensifies hypertensive renal damage.

Hall et al [21] in their review article about Obesity,hypertension,and chronic renal disease,concluded that obesity induces a cascade of changes within the kidney and neurohormonal alteration that lead to impairment in renal pressure natriuresis,high sodium reabsorption,elevated bloodpressure and renal damage.

Yi-Jing Sheen and Wayne Huey-Herng Shew [57] in their review article,mentioned about the risk factors for type-4 cardio-renal syndrome which included diabetes mellitus, hypertension, low HDL cholesterol, physical inactivity, non-traditional risk factors like albuminuria, oxidative stress, increased sympathetic tone.

Ana Karina et al [58] conducted a cross-sectional study and observed that BMI and WC were not associated with e GFR based on serum creatinine and cystatin-C, only Visceral Fat Area was associated with decrease in e GFR.

Kambham et al [59] in an article suggested the link incidence of obesity and risk of obesity-related glomerulopathy.

Chi Yuan Hsu et al [60] in their large Cohart study about BMI and risk for ESRD, they observed a graded strong relationship between the risk for ESRD and high BMI.

" Obesity induced hypertension in the dogs " was conducted by **Albert et al .** [28] In this study nine adult dogs were fed with beef fat for five weeks to increase weight and suggested increase weight was associated with increase in heart rate, BP, cardiac output, plasma volume, fasting insulin concentration.

Pinto Sietsma SJ et al [19] in their study they observed microalbuminuria (MA) was associated with abnormal renal function in non-diabetic individuals.

In their study about central obesity and hypertension **Scaglione R.et al** [61], they found that both in normotensive and hypertensive subjects ,those with central obesity had elevated urine albumin excretion rate than with peripheral obesity.

Chang Y et al [62]in 2006 conducted a study on abdominal obesity, SBP, MA in normotensive and euglycemic Korean men and found that SBP was an independent predictor of microalbuminuria.

Association of WC and BMI with all cause mortality in CKD was studied by **Krammer H et all .** [63]In that study higher mortality was associated with higher WC and not associated with high BMI.

MATERIALS AND METHODS :

This case-control study was conducted in the Department of Physiology, Thanjavur Medical College Hospital, Thanjavur.

Forty normal healthy subjects and forty Hypertensive Chronic Kidney Disease (HT-CKD, Stage I – II) patients were recruited from Thanjavur Medical College Hospital, Thanjavur, in the age group of between > 18 years and < 70 years , study was conducted between June 2015 and May 2016.

Before starting our study, we obtained ethical committee approval and clearance from the college. Informed written consent was obtained from all the subjects who were participating in this study. The purpose of this study was explained clearly in their regional language. The history of the subjects was obtained and noted in a separate pro-forma.

Inclusion Criteria :

- Chronic kidney disease (Stage 1-2)
- Hypertension
- Non-diabetic
- Free from cardiovascular complications

Exclusion Criteria :

- History of any malignancy
- History of or presence of inflammation

- Presence of major cardiovascular event like CVA,myocardial infarction,acute IHD during last three months prior to the study
- Diabetes mellitus
- Heart failure
- Heriditary renal disease

Detailed clinical history was evaluated and Physical examination was done for every participants.

Anthropometric measures like height (in meters), weight (in kilograms) ,waist circumference (in centimeters) and hip circumference (in centimeters) were measured.

Waist Circumference (in centimeters) : [64]

Waist circumference was measured at the midpoint between the lower margin of least palpable rib and the top of iliac crest at the end of normal expiration in standing position with arms at the sides and feet positioned closed together .The optimal waist circumference for males < 90 cm and for females < 80 cm for South-Asian ethnic groups. WC is an important measurement of central obesity.

Hip circumference (in centimeters) : [64]

Hip circumference (HC) was measured around the widest portion of the buttocks with tape parallel to the floor.

BMI (in Kg / m^2) :

BMI was calculated by dividing weight in Kg by height in meter square,Waist hip ratio (WHR) was calculated by dividing waist circumference by hip circumference and WHR is expressed in centimeters.The normal BMI range is 5 – 24.9 Kg / m^2.

Bloodpressure (BP in mmHg) measurement: [33]

BP is a dynamic physiological function and it varies with each heart beat. For measurement of blood pressure(BP) appropriate size cuff is important. Appropriate size cuff was selected based on mid arm circumference (MAC) of the participants. Based on MAC and bladder dimension in **American Heart Association Guidelines** the following cuff sizes are recommended :

Small adult MAC range 22 – 27.5 cm, width 12 cm, length 22 cm ;

Adult MAC range 30 – 37.5 cm, width 16 cm, length 30 cm ;

Large adult range 38 – 47.5 cm, width 16 cm, length 38 cm ;

The blood pressure was measured in a quiet and relaxed setting after five minutes of rest with feet relaxed and flat on the floor .The participants were seated with their back against chair and the arm wearing cuff was supported at the elbow and was kept at the level of heart .The cuff was tied 2.5 cm above the cubital fossa. The blood pressure was measured by palpatory method followed by using mercury sphygmomanometer. The cuff was deflated at a rate of 2 – 4 mmHg/sec in the auscultatory method, appearance of Korotkoff sound (phase I) was considered as

systolic blood pressure (SBP) and disappearance of Korotkoff sound (phase IV) was considered as diastolic blood pressure (DBP).

European Society of Cardiology Guidelines for management of Hypertension and Joint National Committee Guidelines for Detection, Evaluation and Management of Hypertension defined hypertension as SBP ≥ 140 mmHg and DBP ≥ 90 mmHg.

Serum creatinine estimation (in mg / dl) : [44]

For serum creatinine estimation, 5 ml of venous blood was taken in the red –topped (serum separator) tube from the medial cubital vein in the anti-cubital fossa of the participants under sterile condition. Serum creatinine was measured by using **Jaffe's kinetic method** by using auto analyzer. The normal range of serum creatinine for males 0.6 – 1.2 mg/dl, and for females 0.4 – 1.0mg/dl.

Blood urea estimation (in mg / dl): [44,65]

For the blood urea estimation, to get 5 ml of venous blood, a sterile needle was gently guided in the anti-cubital vein of the participants after cleaning the skin of puncture site and was estimated by **enzymatic (kinetic) method** by using autoanalyzer .

The normal range is 15 – 45 mg / dl.

24-hours urine Albumin Excretion Rate (AER in mg/24 hrs): [44,48,65]

Then to assess renal function 24-hours urine was collected for the estimation of Albumin Excretion Rate (AER).The importance of the test was explained clearly to the participants. Heavy physical work and high protein diet intake were restricted on

the previous day and the day of urine collection. Normal fluids and food intake was allowed. Fluids was not forced to avoid of very diluted urine. The participants were asked to empty the bladder completely on awakening and discard the first urine specimen and all the urine voided over the next 24 hours was collected in a large sterile container which contained a preservative (thymol) to reduce bacterial action or chemical decomposition. This 24 hours urine collection was delivered to the laboratory without delay. Normal AER is < 30 mg .

Microalbuminuria is defined as 30 – 300 mg albumin excretion / 24 hours urine. Macroalbuminuria is defined as urine albumin excretion > 300 mg / day.

e GFR (ml/min/1.73m^2) :

GFR was estimated by using MDRD formula, [16, 20]

e GFR (ml/min/1.73m^2) = 186 × [Serum Creatinine level]$^{-1.154}$ × [Age]$^{-0.203}$ × [0.742 if patient is female] × [1.212 if the patient is black].

The normal average GFR is 125 ml / min. Normal glomerular filtration rate (GFR) ranges from 90 – 140 ml / min for adult male and ranges from 80 – 125 ml / min in females. [39]

Thus the anthropometric and renal function parameters were measured to compare the effect of BMI and waist circumference on renal function decline in hypertensive chronic kidney disease.

The following instruments were used in this study :

1. Auto-Analyzer(BECKMAN COUTLER,AU – 480)
2. Urine analyzer (COBOS 6000-HITACHI)
3. LIQUIXX Urea (BUN) Kit for blood urea estimation
4. LIQUIXX Creatinine Kit for serum creatinine estimation
5. Weighing machine (KRUPS)
6. Sphygmomanometer (DIAMOND)
7. Stethoscope (MICROTONE)
8. Sterile container for urine collection and preservative (Thymol)
9. Test tubes for blood collection
10. Inch tape
11. Miscellaneous things like spirit, cotton, syringes, needles.

Figure–5.Auto Analyser for urea and creatinine.(BECKMAN COUTLER,AU – 480).

Figure – 6.Auto Analyser for 24-hrs urine AER.(COBOS 6000-HITACHI).

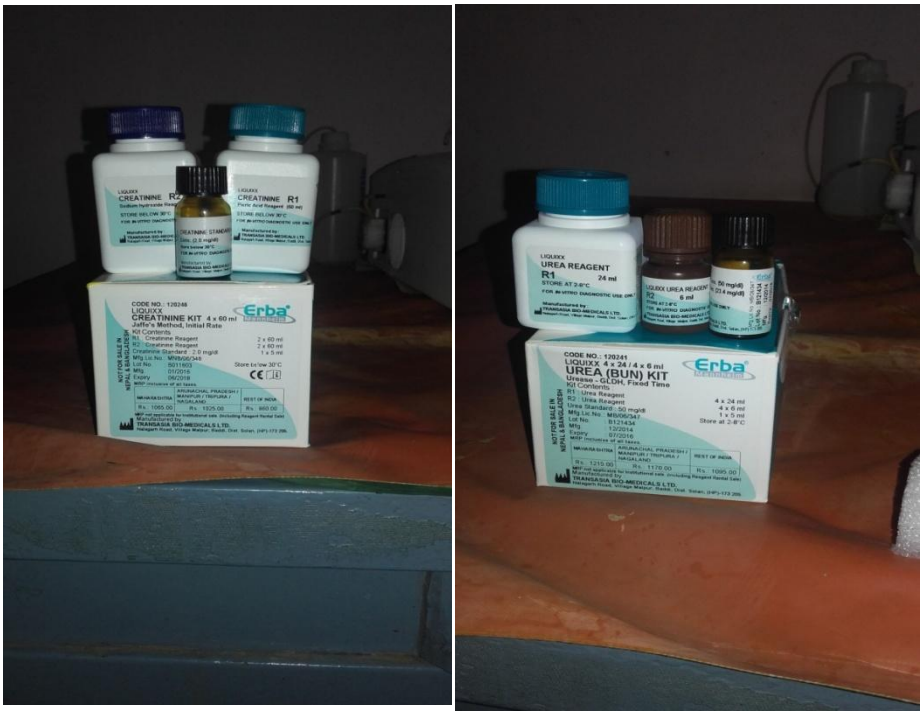

Figure-7. LIQUIXX Urea (BUN) Kit for blood urea estimation

LIQUIXX Creatinine Kit for serum creatinine estimation

Figure-8. Weighing machine, inch tape, sphygmomanometer, stethoscope.

Figure–9.Other materials used in this study (Red topped test tubes, syringes, cotton, container for urine collection and its preservative.)

In this study, thymol was used as preservative for 24 hours urine collection to prevent bacterial growth which may affect the expected result.

Other urine preservatives :[65]

PRESERVATIVES	**CONCENTRATION / VOLUME**
HCl	6mol /L;30 ml/24 hr collection
Acetic acid	50%;25 ml / 24 hr collection
Na_2CO_3	5g / 24 hr collection
HNO_3	6 mol/ L; 15ml/ 24 hr collection
Baric acid	10 g/ 24 hr collection
Toluene	30 ml / 24 hr collection
Thymol	10 % in isopropanol;10 ml /24 hr collection.

RESULTS

In this case-control study which was conducted in Thanjavur Medical College,control group consisted fourty healthy adults ;and the study group included fourty hypertensive chronic kidney disease (stage I – II) patients.In the study group,Group 1- included patients with normal waist circumference and normal BMI,Group 2-included patients with high waist circumference and normal BMI,Group 3-included patients with normal waist circumference and high BMI.

Statistical analysis was done by using the Statistical Package for Social Sciences (SPSS) X version.The results were analyzed by using student 't' test and ANOVA study.Datas are expressed in mean with standard deviation.Correlation of BMI and WC,WHR with various renal function by using Pearson's Correlation test.

$P < 0.05$ was considered as statistically significant.

Descriptive analysis was done for all the parameters and are tabulated in Table-1.

The parameters are age, height, weight, systolic blood pressure, diastolic blood pressure, BMI, waist circumference, WHR, urea, creatinine, AER and e GFR.

TABLE - 1

DESCRIPTIVE STATISTICS

CLINICAL PARAMETERS OF CONTROL AND STUDY GROUPS

Parameters	Study HT-CKD (n=40)				Control (n=40)				Total subjects (n=80)			
	Min.	Max.	Mean	S.D	Min.	Max.	Mean	S.D	Min.	Max.	Mean	S.D
Age (yrs)	38	53	43.88	3.568	38	52	46.28	3.796	38	53	45.08	3.854
SBP (mmHg)	130	150	141.90	4.199	100	130	117.05	7.089	100	150	129.47	13.779
DBP (mmHg)	86	96	89.95	2.660	70	84	78.95	3.328	70	96	84.45	6.292
Height(m)	1.50	1.68	1.5903	.03820	1.51	1.72	1.6103	.05127	1.50	1.72	1.6003	.04603
Weight(Kg)	52	73	59.95	5.383	50	64	55.83	2.978	50	73	57.89	4.794
BMI(Kg/m^2)	19.10	28.70	23.760	2.30549	2.30	24.40	21.1357	3.36847	2.30	28.70	22.4479	3.15736
WC(cm)	76	110	88.95	8.750	76	86	82.10	2.362	76	110	85.53	7.241
HC(cm)	82	110	96.58	5.509	76	98	85.02	4.764	76	110	90.80	7.743
WHR	.83	1.08	.9230	.07505	.83	1.03	.9388	.04821	.83	1.08	.9309	.06317
Urea(mg/dl)	41	62	51.10	6.172	12	32	21.32	4.323	12	62	36.21	15.889
Creatinine (mg/dl)	.86	1.22	1.0620	.11654	.40	.73	.5823	.09113	.40	1.22	.8221	.26282
eGFR(ml/min/1.73 m^2)	60	85	69.05	8.779	103	217	139.57	27.817	60	217	104.31	40.978
AER(mg/24 hrs)	35	190	76.05	41.121	3	14	6.42	3.38	3	190	41.23	45.47

The result shown in Table-1 are as follows :

The mean age of control group was 46.28 ± 3.79 yrs

The mean age of study group was 43.88 ± 3.56 yrs

The mean height of control group was 1.61 ± 0.05 m

The mean height of study group was 1.59 ± 0.03 m

The mean weight of control group was 55.822 ± 2.97 Kg

The mean weight of study group was 59.95 ± 5.38 Kg

The systolic and diastolic blood pressure of the control and the study groups-1,2,3 are expressed in mean ± standard deviation in Table – 2.

The mean SBP of control group was 117.05 ± 7.08 mmHg

The mean SBP of study group-1 was 141.57 ± 5.33 mmHg

The mean SBP of study group-2 was 142.71 ± 3.64 mmHg

The mean SBP of study group-3 was 141.33 ± 3.44 mmHg

The mean DBP of control group was 78.95 ± 3.32 mmHg

The mean DBP of study group-1 was 90.14 ± 2.98 mmHg

The mean DBP of study group-2 was 90.57 ± 2.87 mmHg

The mean DBP of study group-3 was 89.0 ± 1.80 mmHg

TABLE – 2

SYSTOLIC AND DIASTOLIC BLOOD PRESSURE OF CONTROL AND STUDY GROUPS

PARICIPANTS		SBP (mmHg)	DBP (mmHg)
CONTROL GROUP	N	40	40
	Mean	117.05	78.95
	SD	7.08	3.32
STUDY GROUP-1	N	14	14
	Mean	141.57	90.14
	SD	5.33	2.98
STUDY GROUP-2	N	14	14
	Mean	142.71	90.57
	SD	3.64	2.87
STUDY GROUP-3	N	12	12
	Mean	141.33	89.00
	SD	3.44	1.80

TABLE -3

DESCRIPTIVE ANALYSIS OF SBP & DBP IN STUDY AND CONTROL GROUPS

Bloodpressure	Mean	S.D	T	DF	Statistical inference
SBP(mmHg)					
Study group (N=40)	141.90	4.199	19.075	78	.000<0.05 Significant
Control group(N=40)	117.05	7.089			
DBP(mmHg)					
Study group (N=40)	89.95	2.660	16.331	78	.000<0.05 Significant
Control group(N=40)	78.95	3.328			

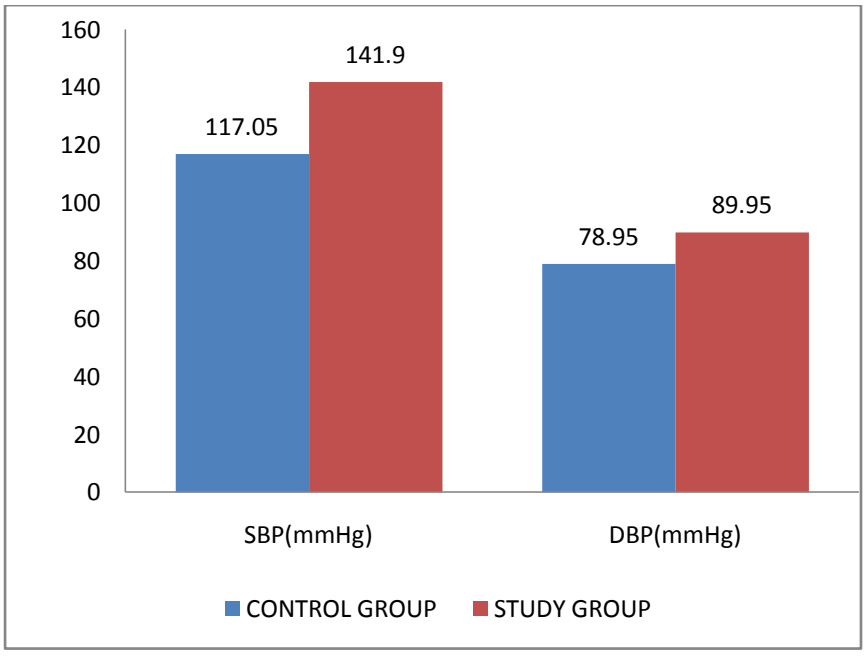

Figure-11.Comparison of SBP,DBP between control & study groups.

Table-3 and Figure-11 show the comparison of SBP and DBP in the study and the control groups. Mean SBP and the mean DBP between study and control groups were statistically more significant.

Analysis of SBP and DBP between study group-1,group-2,group-3 by using ANOVA study are shown in Table 4. The mean difference of SBP and DBP between study group-1,group-2,group-3 were not statistically significant.

TABLE -4

ANALYSIS SBP & DBP BETWEEN STUDY GROUPS BY ANNOVA STUDY

BLOODPRESSURE	Mean	SD	SS	Df	MS	F	Statistical Inference
SBP(mmHg)							
Between Groups			**14.648**	**2**	**7.324**	**.403**	**.671>0.05 Not Significant**
Group-1(N=14)	**141.57**	**5.331**					
Group-2(N=14)	**142.71**	**3.646**					
Group-3(N=12)	**141.33**	**3.447**					
Within Groups			**672.952**	**37**	**18.188**		
DBP(mmHg)							
Between Groups			**16.757**	**2**	**8.379**	**1.196**	**.314>0.05 Not Significant**
Group-1(N=14)	**90.14**	**2.983**					
Group-2(N=14)	**90.57**	**2.875**					
Group-3(N=12)	**89.00**	**1.809**					
Within Groups			**259.143**	**37**	**7.004**		

TABLE -5

DESCRIPTIVE ANALYSIS OF WEIGHT ,BMI,WC,HC IN STUDY AND CONTROL GROUPS

Parameters	Mean	S.D	T	Df	Statistical inference
WEIGHT(Kg)					
Study group (N=40)	**59.95**	**5.383**	**4.241**	**78**	**.000<0.05 Significant**
Control group(N=40)	**55.82**	**2.978**			
BMI(Kg/m^2)					
Study group (N=40)	**23.7600**	**2.30549**	**4.066**	**78**	**.000<0.05 Significant**
Control group(N=40)	**21.1358**	**3.36847**			
WC(cm)					
Study group (N=40)	**88.95**	**8.750**	**4.780**	**78**	**.000<0.05 Significant**
Control group(N=40)	**82.10**	**2.362**			
HC(cm)					
Study group (N=40)	**96.58**	**5.509**	**10.030**	**78**	**.000<0.05 Significant**
Control group(N=40)	**85.03**	**4.764**			

The comparison of weight(Kg),waist circumference(cm),hip circumference(cm),waist hip ratio are shown in Table-5 and Figure- 12

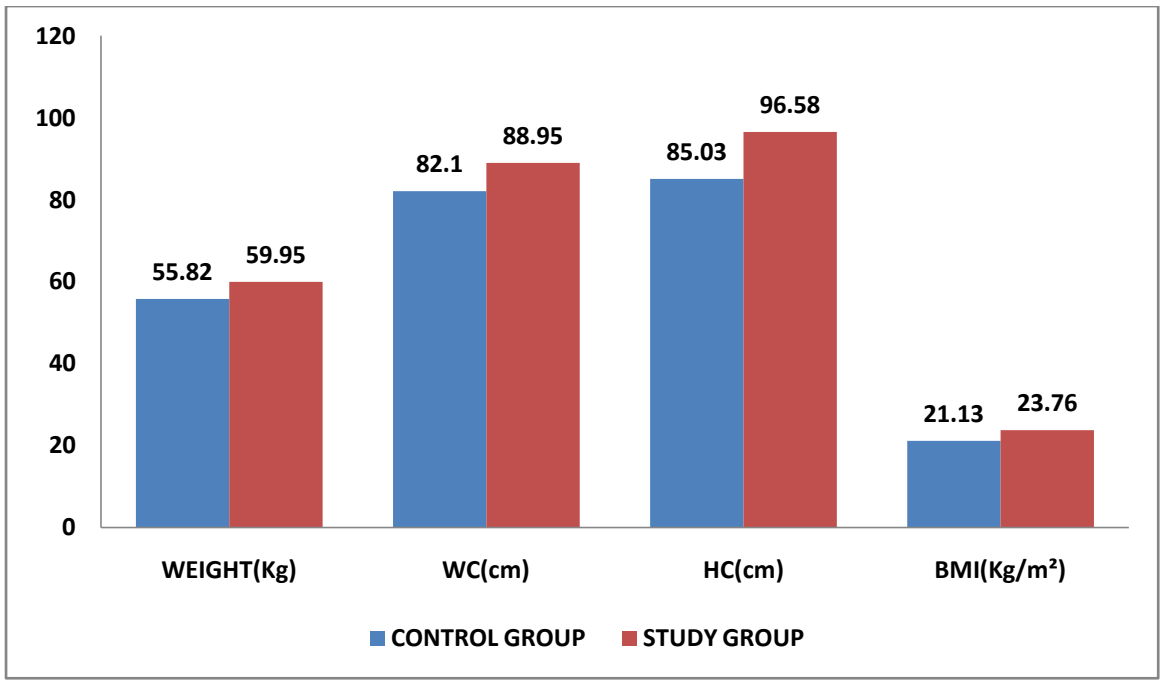

Figure-12.Comparison of Weight,WC,HC,BMI between control and study groups.

The mean weight of the control group was 55.82 ± 2.978 Kg. The mean weight of the study group was 59.95 ± 5.383 Kg

The mean BMI of the control group was 21.13 ± 3.36 Kg/m^2The mean BMI of the study group was 23.76 ± 2.30 Kg/m^2

The mean WC of the control group was 82.10 ± 2.36 cm.The mean WC of the study group was 88.95 ± 8.75 cm

The mean HC of the control group was 85.03 ± 4.76 cm. The mean HC of the study group was 96.58 ± 5.50 cm

The mean weight, BMI, WC, HC between the control and the study groups were statistically significant.

TABLE – 6

BMI,WC,HC,WHR OF CONTROL AND STUDY GROUPS

PARICIPANTS		BMI(Kg/m^2)	WC(cm)	HC(cm)	WHR
CONTROL GROUP	N	40	40	40	40
	Mean	21.13	82.10	85.02	0.93
	SD	3.36	2.36	4.76	0.04
STUDY GROUP-1	N	14	14	14	14
	Mean	21.84	81.93	93.36	0.87
	SD	1.18	2.37	5.19	0.03
STUDY GROUP-2	N	14	14	14	14
	Mean	23.11	100.0	100.86	1.00
	SD	0.97	3.86	4.64	0.05
STUDY GROUP-3	N	12	12	12	12
	Mean	26.75	84.25	95.33	0.88
	SD	1.06	2.22	3.47	0.02

Mean ± Standard deviation of obesity parameters (Weight, BMI, WC, HC,WHR) of the study group (Group-1, Group-2, Group-3) and the control group are represented in Table -6

The mean BMI of study group-3 was 26.75 ± 1.05 Kg / m². The mean WC of study group-2 was 100 ± 3.86 cm.

TABLE -7

ANALYSIS OF WEIGHT, BMI, WC, HC, WHR BETWEEN STUDY GROUPS BY ANOVA STUDY

Parameters	Mean	S.D	SS	Df	MS	F	Statistical inference
WEIGHT(Kg)							
Between Groups			**845.215**	**2**	**422.67**	**54.869**	**.000<0.05 Significant**
Group-1(N=14)	**56.29**	**2.091**					
Group-2(N=14)	**57.64**	**1.216**					
Group-3(N=12)	**66.92**	**4.358**					
Within Groups			**284.976**	**37**	**7.702**		
BMI(Kg/m^2)							
Between Groups			**164.572**	**2**	**82.287**	**71.267**	**.000<0.05 Significant**
Group-1(N=14)	**21.8429**	**1.17912**					
Group-2(N=14)	**23.1143**	**.97417**					
Group-3(N=12)	**26.7500**	**1.05787**					
Within Groups			**42.721**	**37**	**1.155**		
WC(cm)							
Between Groups			**2664.441**	**2**	**1332.220**	**153.455**	**.000<0.05 Significant**
Group-1(N=14)	**81.93**	**2.369**					
Group-2(N=14)	**100.00**	**3.863**					
Group-3(N=12)	**84.25**	**2.221**					
Within Groups			**321.215**	**37**	**8.681**		
HC(cm)							
Between Groups			**420.180**	**2**	**210.090**	**10.180**	**.000<0.05 Significant**
Group-1(N=14)	**93.36**	**5.198**					
Group-2(N=14)	**100.86**	**4.639**					
Group-3(N=12)	**95.33**	**3.473**					
Within Groups			**763.595**	**37**	**20.638**		
WHR							
Between Groups			**.150**	**2**	**.075**	**39.799**	**.000<0.05 Significant**
Group-1(N=14)	**.8771**	**.03750**					
Group-2(N=14)	**1.0064**	**.05930**					
Group-3(N=12)	**.8792**	**.02275**					
Within Groups			**.070**	**37**	**.002**		

Analysis of weight, body mass index, waist circumference, hip circumference, waist hip ratio of study groups by ANOVA study is tabulated in Table-7.

The mean difference of these values (Weight, BMI, WC, HC, WHR) were statistically significant between and within the study groups.

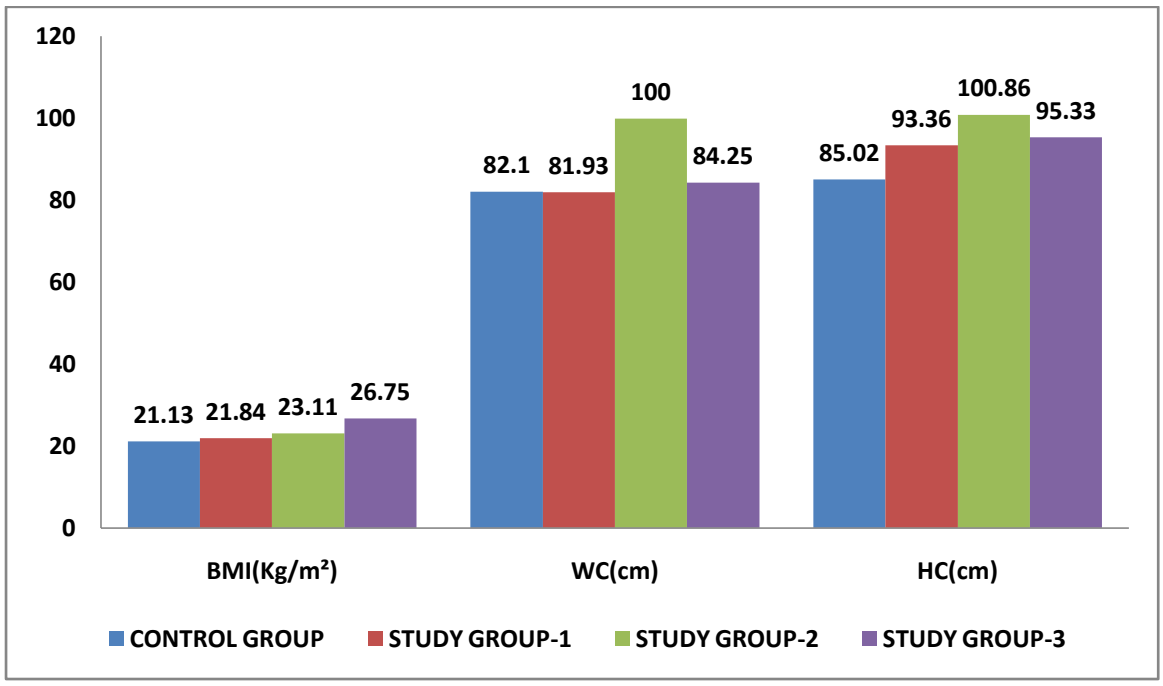

Figure-13. Comparison of BMI, WC, HC between control and Group-1, Group-2 and Group-3 of study groups.

The mean BMI of study group-3 (26.75 ± 1.06 Kg/m^2) was more than that of study group-2 (23.11 ± 0.97 Kg/m^2) and study group-1 (21.84 ± 1.18 Kg/m^2) which was statistically significant $P < 0.05$.

The WC of study group-2 (100.0 ± 3.86 cm) was statistically significantly ($P < 0.05$) high than that of study group-1 (81.93 ± 2.37 cm) and study group-3 (84.25 ± 2.22 cm) .

Table-8 and the Figures- 14-16 show the comparison of blood urea,serum creatinine levels,e GFR and AER of the study and control groups.

TABLE -8

DESCRIPTIVE ANALYSIS OF UREA,CREATININE, e GFR,AER IN STUDY AND CONTROL GROUPS

Parameters	Mean	S.D	T	Df	Statistical inference
Urea(mg/dl)					
Study group (N=40)	**51.10**	**6.172**	**24.991**	**78**	**.000<0.05 Significant**
Control group(N=40)	**21.33**	**4.323**			
Creat(mg/dl)					
Study group (N=40)	**1.0620**	**.11654**	**20.510**	**78**	**.000<0.05 Significant**
Control group(N=40)	**.5823**	**.09113**			
e GFR(ml/min/1.73m^2)					
Study group (N=40)	**69.05**	**8.779**	**-15.291**	**78**	**.000<0.05 Significant**
Control group(N=40)	**139.57**	**27.817**			
AER(mg/24 hrs)					
Study group (N=40)	**76.05**	**41.121**	**9.496**	**78**	**.000<0.05 Significant**
Control group(N=40)	**6.42**	**3.38**			

The mean blood urea of the control group was 21.33 ± 4.32 mg/dl

The mean blood urea of the study group was 51.10 ± 6.17 mg/dl

The mean serum creatinine of the control group was 0 .58 ± .09 mg/dl.The mean serum creatinine of the study group was 1.06 ± 0.12 mg/dl

The mean blood urea and the mean serum creatinine between study and control groups were statistically more significant.

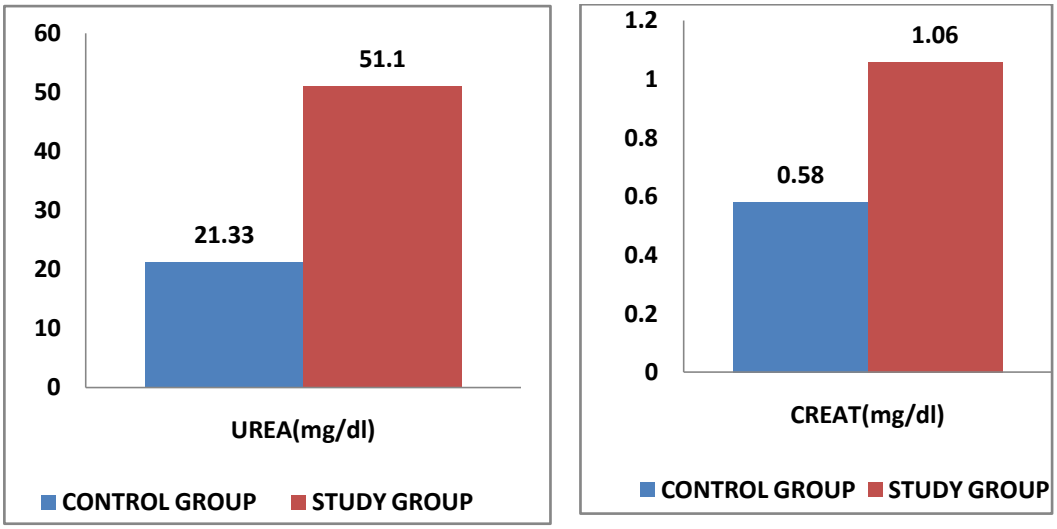

Figure-14 &15.Comparison of urea between control & study group and of creatinine between the same two groups respectively.

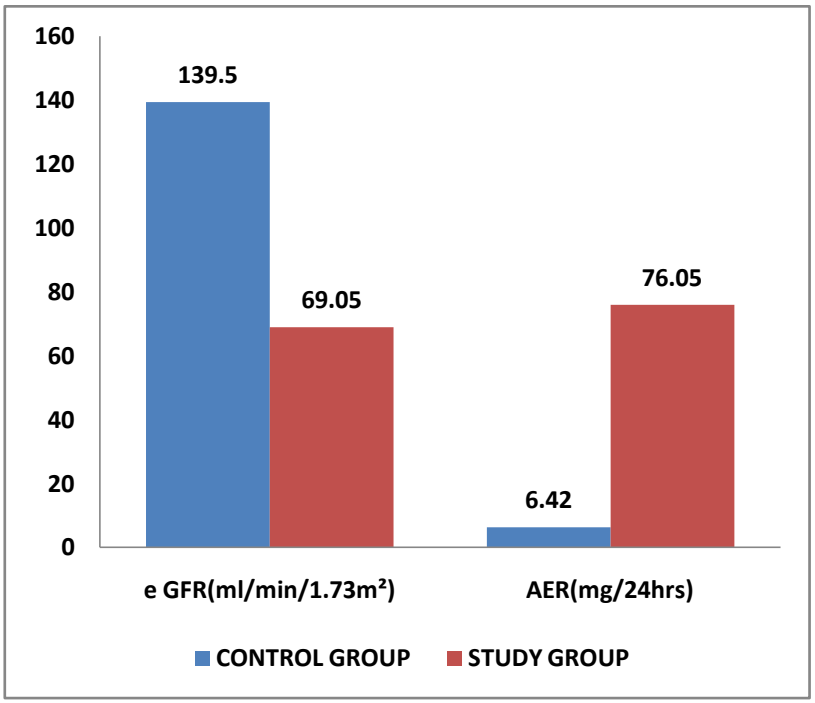

Figure-16. Comparison of e GFR & AER between control and study groups

The mean e GFR of the control group was 139.57 ± 27.81 ml/min/1.73m^2

The mean e GFR of the study group was 69.05 ± 8.78 ml/min/1.73m^2

The mean AER of the control group was 6.42 ± 3.38 mg/24 hrs

The mean AER of the study group was 76.05 ± 41.12 mg/24 hrs

The mean e GFR and the mean AER between study and control groups were statistically more significant.

Analysis of blood urea and serum creatinine levels between and within the study groups were done and are shown in Table-9 and between study and control groups are tabulated and are shown in Table - 10.The mean values of all groups are plotted in figures 17 & 18.

TABLE -9

ANALYSIS OF UREA, CREATININE BETWEEN STUDY GROUPS BY ANOVA STUDY

Parameters	Mean	S.D	SS	Df	MS	F	Statistical inference
UREA(mg/dl)							
Between Groups			**398.163**	**2**	**199.081**	**6.791**	**.003<0.05 Significant**
Group-1(N=14)	**47.79**	**5.236**					
Group-2(N=14)	**50.57**	**5.840**					
Group-3(N=12)	**55.58**	**5.107**					
Within Groups			**1086.673**	**37**	**29.370**		
CREAT(mg/dl)							
Between Groups			**.387**	**2**	**.193**	**50.086**	**.000<0.05 Significant**
Group-1(N=14)	**.9350**	**.08309**					
Group-2(N=14)	**1.1664**	**.04217**					
Group-3(N=12)	**1.0883**	**.05219**					
Within Groups			**.143**	**37**	**.004**		

The mean serum creatinine of study group-1 was 0.93 ± 0.08 mg/dl

The mean serum creatinine of study group-2 was 1.16 ± 0.04 mg/dl

The mean serum creatinine of study group-3 was 1.08 ± 0.05 mg/dl.

The mean serum creatinine of Group-2 (1.16 ± 0.04mg/dl) was higher than Group-3 (1.08 ± 0.05mg/dl) and Group-1(0.93 ± 0.08mg/dl).

The mean blood urea level of Group-3 (55.58 ± 5.11 mg/dl) was higher than Group-1 (47.79 ± 5.24 mg/dl) and Group-2(50.57 ± 5.84 mg/dl).

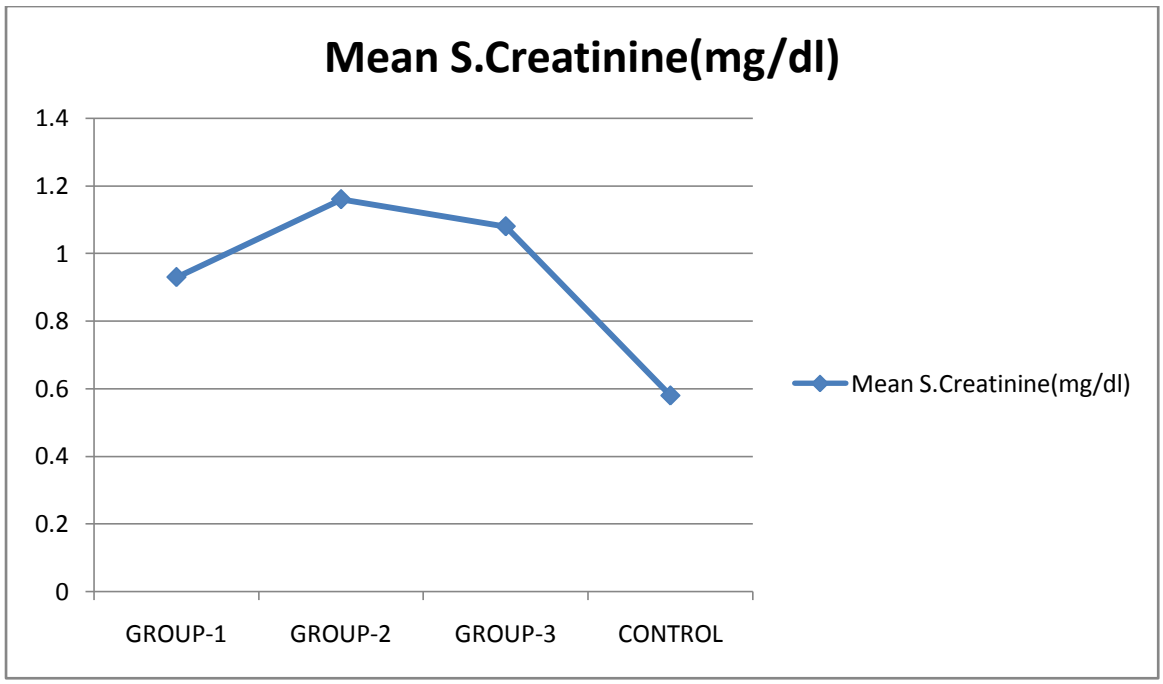

Figure – 17.Mean S.Creatinine levels in study groups and control group.

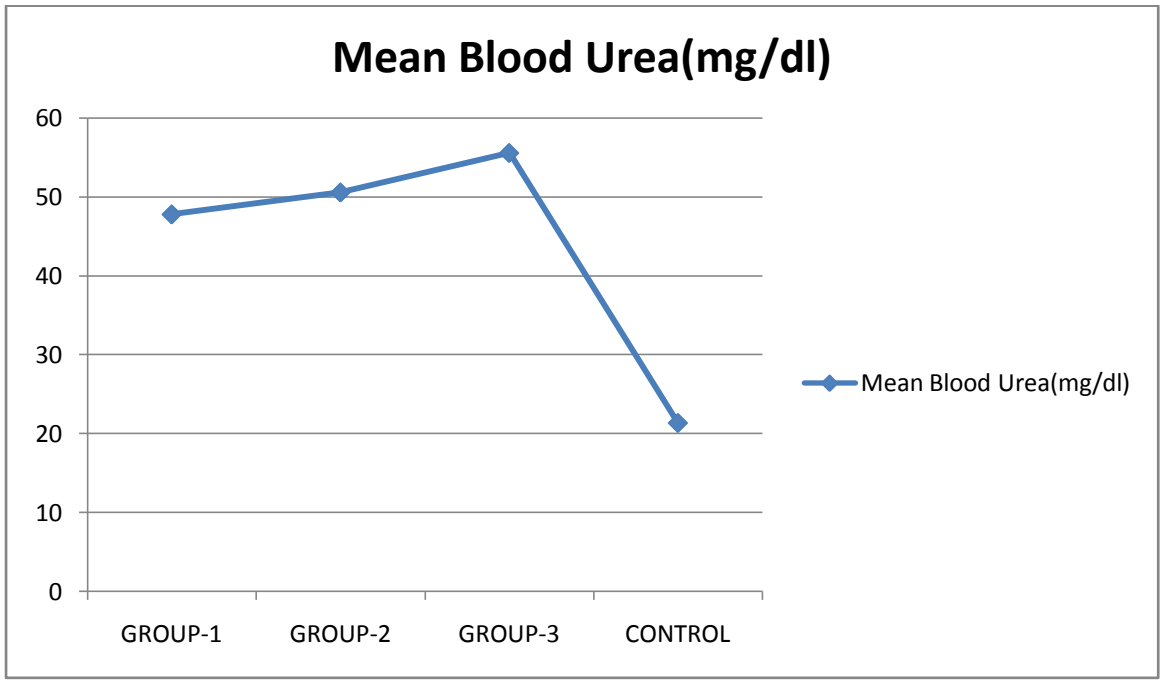

Figure – 18.Mean blood Urea levels in study groups and control group.

TABLE – 10

UREA AND CREATININE OF CONTROL AND STUDY GROUPS

PARICIPANTS		UREA(mg/dl)	CREAT(mg/dl)
CONTROL GROUP	N	40	40
	Mean	21.33	0.58
	SD	4.32	0.09
STUDY GROUP-1	N	14	14
	Mean	47.79	0.93
	SD	5.23	0.08
STUDY GROUP-2	N	14	14
	Mean	50.57	1.16
	SD	5.84	0.04
STUDY GROUP-3	N	12	12
	Mean	55.58	1.08
	SD	5.10	0.05

Analysis of e GFR and AER between and within the study and the control groups were done and is shown in Table-11 and 12. The mean values are depicted in figures 19 - 21.

TABLE – 11

eGFR AND AER OF CONTROL AND STUDY GROUPS

PARICIPANTS		eGFR(ml/min/1.73m^2)	AER(mg/24 hrs)
CONTROL GROUP	N	40	40
	Mean	139.57	6.42
	SD	27.81	3.38
STUDY GROUP-1	N	14	14
	Mean	78.71	45.0
	SD	6.95	6.61
STUDY GROUP-2	N	14	14
	Mean	61.36	115.29
	SD	1.59	42.77
STUDY GROUP-3	N	12	12
	Mean	66.75	66.50
	SD	3.621	22.25

TABLE -12

ANALYSIS OF e GFR, AER BETWEEN STUDY GROUPS BY ANOVA STUDY

Parameters	Mean	S.D	SS	Df	MS	F	Statistical inference
eGFR(ml/min/1.73m^2)							
Between Groups			**2199.579**	**2**	**1099.789**	**50.466**	**.000<0.05 Significant**
Group-1(N=14)	**78.71**	**6.955**					
Group-2(N=14)	**61.36**	**1.598**					
Group-3(N=12)	**66.75**	**3.621**					
Within Groups			**806.321**	**37**	**21.792**		
AER(mg/24 hrs)							
Between Groups			**36144.043**	**2**	**18072.021**	**22.437**	**.000<0.05 Significant**
Group-1(N=14)	**45.00**	**6.610**					
Group-2(N=14)	**115.29**	**42.776**					
Group-3(N=12)	**66.50**	**22.253**					
Within Groups			**29801.857**	**37**	**805.456**		

The mean e GFR of the control group was 139.57 ± 27.81 ml/min/1.73m^2

The mean e GFR of study Group-1(78.71 ± 6.95 ml/min/1.73m^2) was higher than study Group-2(61.36 ± 1.59ml/min/1.73m^2) and study Group-3 (66.75 ± 3.62ml/min/1.73m^2) which was statistically significant $P < 0.05$.

The mean AER of the control group was 6.42 ± 3.38 mg/24 hrs.

The mean AER of study Group-2(115.29 ± 42.77 mg/24 hrs) was statistically significantly($P < 0.05$) higher than study Group-3(66.50 ± 22.25 mg/24 hrs) and study Group-1(45.0 ± 6.61 mg/24 hrs).

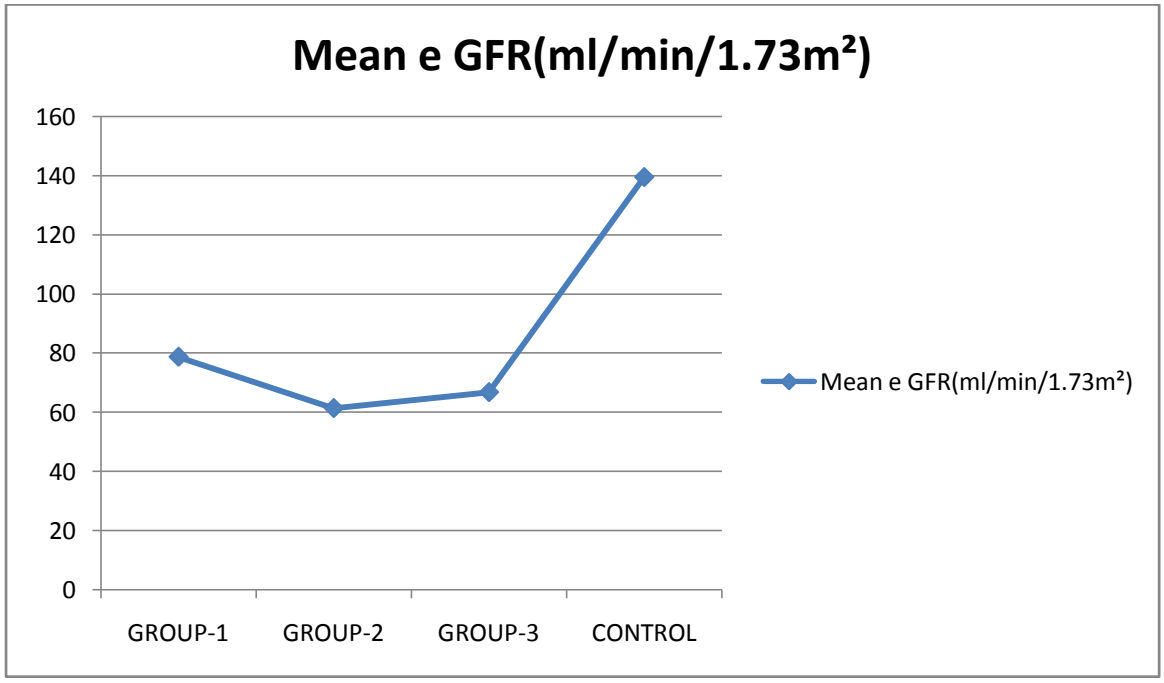

Figure – 19.Mean e GFR levels in study groups and control group.

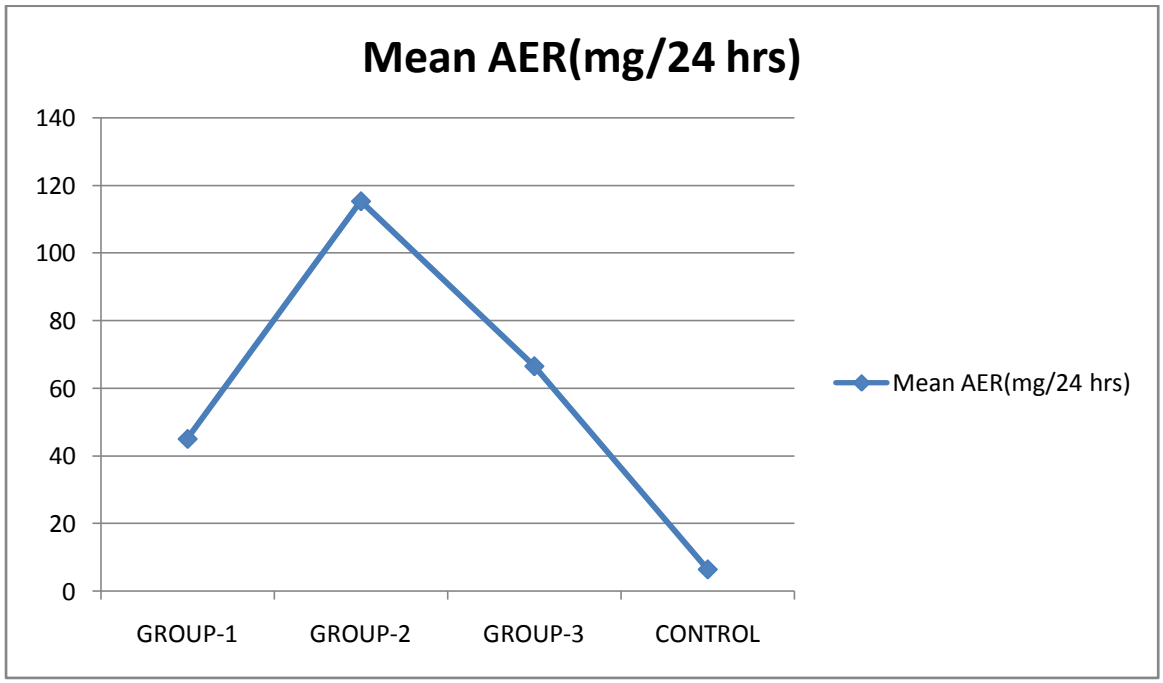

Figure – 20.Mean AER levels in study groups and control group.

The mean e GFR of the study group-3 which had normal WC and high BMI was higher (statistically significant $P < 0.05$) than that of study group-2 which had high WC and normal BMI and the mean e AER of the study group-2 which had high WC and normal BMI was higher (statistically significant $P < 0.05$) than that of study group-3 which had normal WC and high BMI

The mean AER of the study group-1was 45.0 ± 6.61 mg/24 hrs

The mean AER of the study group-2 was 115.29 ± 42.77 mg/24 hrs

The mean AER of the study group-3 was 66.50 ± 22.25 mg/24 hrs

The mean AER of the study group-2 was higher (statistically significant $P < 0.05$) than that of study group-1 and study group-2.

The mean AER of the study group-3 which had normal WC and high BMI was lower(statistically significant $P < 0.05$) than that of study group-2 which had high WC and normal BMI .

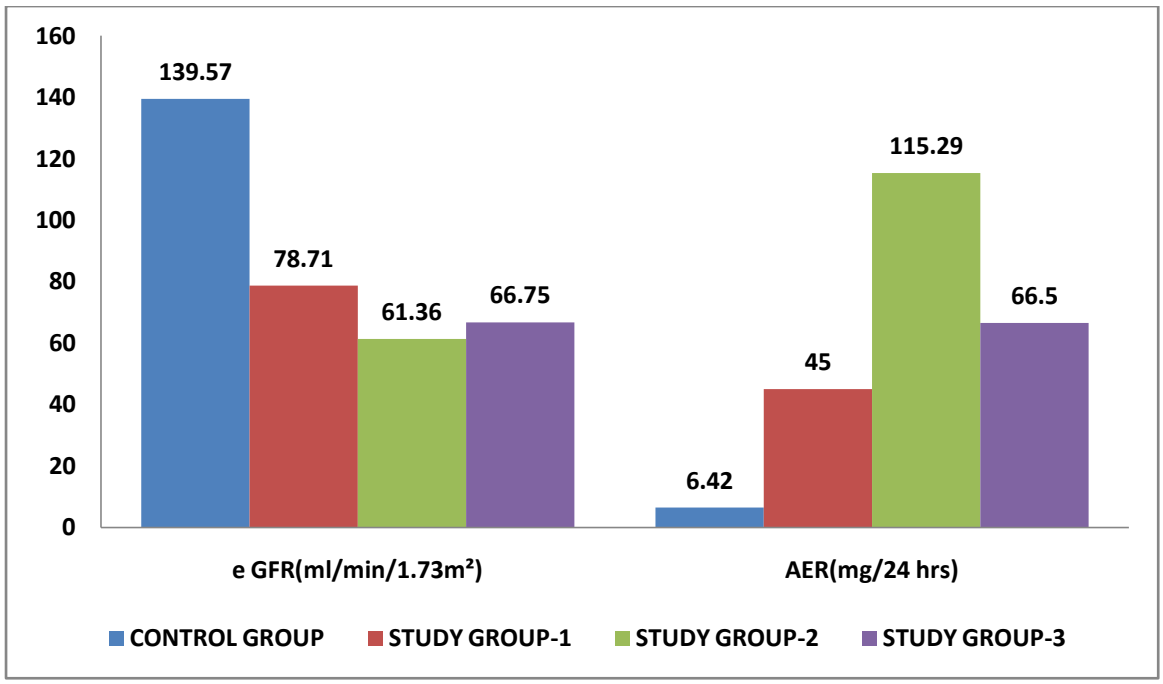

Figure-21. Comparison of e GFR & AER between control and study group-1, study group-2, study group-3.

At the same time renal function decline was more in study group-2 than study group-3..

Microalbuminuria which is defined as AER 30 – 300 mg / 24 hrs urine ,is an important and most sensitive marker of renal damage .High AER in study group-2 in this study indicates that renal damage was more in the study group with high WC that is renal function decline was more with central obesity than with high BMI.

The mean difference of these renal function parameter values (blood urea, serum creatinine, e GFR,AER) were statistically significant between and within the study group.

Table-13 & 14 and figures 22 & 23 show the correlation of BMI with renal function decline of the study group with stage 1-2 HT-CKD.Statistically significant correlation between BMI with e GFR decline (negative correlation) was observed in the study group and also no significant correlation between BMI with serum creatinine level elevation and elevated AER level.There is positive correlation between BMI and blood Urea level.

TABLE-13

STUDY GROUP (N=40)

Correlations of BMI with renal parameters

BMI(Kg/m^2)	**Correlation value**	**Statistical inference**
CREAT(mg/dl)	**.301**	**p>0.05 Not Significant**
e GFR(ml/min/1.73m^2)	**-.320(*)**	**p<0.05 Significant**
AER(mg/24 hrs)	**-.002**	**p>0.05 Not Significant**

* Correlation is significant at the 0.05 level

TABLE-14

STUDY GROUP (N=40)

Correlations of BMI with blood pressure & blood urea

BMI(Kg/m^2)	**Correlation value**	**Statistical inference**
SBP(mmHg)	-.139	p>0.05 Not Significant
DBP(mmHg)	-.273	p>0.05 Not Significant
UREA(mg/dl)	.356(*)	p<0.05 Significant

* Correlation is significant at the 0.05 level

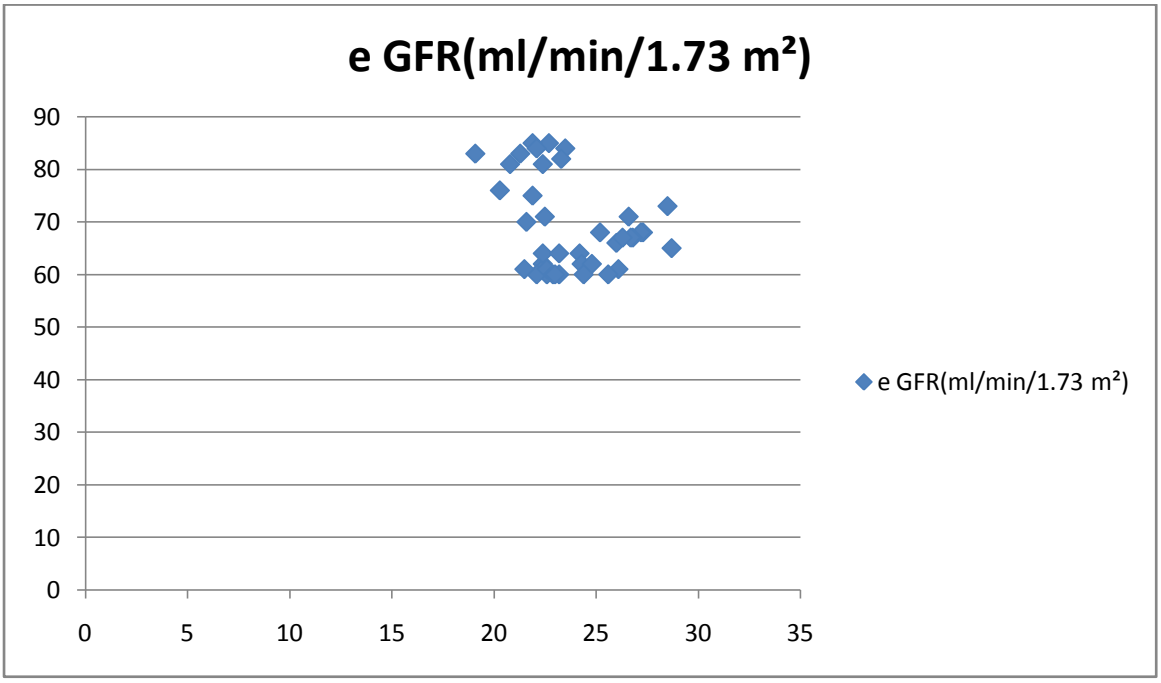

Figure – 22. Negative correlation of BMI with e GFR

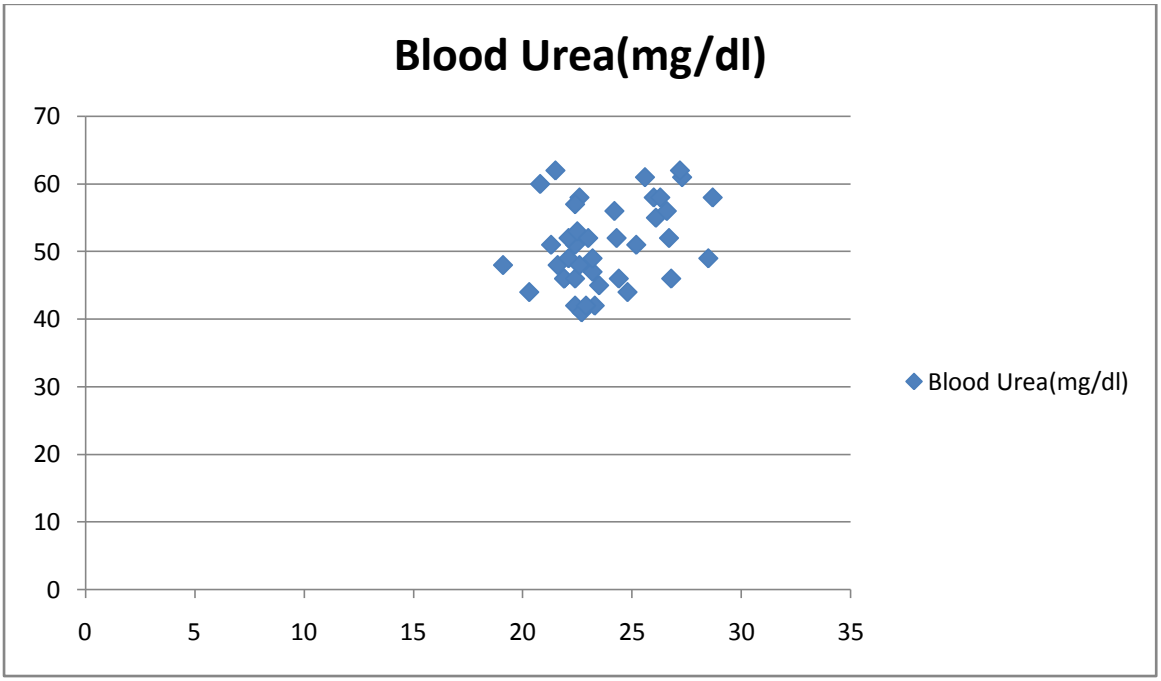

Figure – 23.Positive correlation of BMI with blood urea level

TABLE-15

STUDY GROUP (N=40)

Correlations of WC with renal parameters

WC(cm)	Correlation value	Statistical inference
CREAT(mg/dl)	**.675(**)**	**p<0.01 Significant**
e GFR(ml/min/1.73m^2)	**-.689(**)**	**p<0.01 Significant**
AER (mg/24 hrs)	**.685(**)**	**p<0.01 Significant**

** Correlation is significant at the 0.01 level

TABLE-16

STUDY GROUP (N=40)

Correlations of WC with blood pressure & blood urea

WC(cm)	Correlation value	Statistical inference
SBP(mmHg)	-.060	p>0.05 Not Significant
DBP(mmHg)	.176	p>0.05 Not Significant
UREA(mg/dl)	-.073	p>0.05 Not Significant

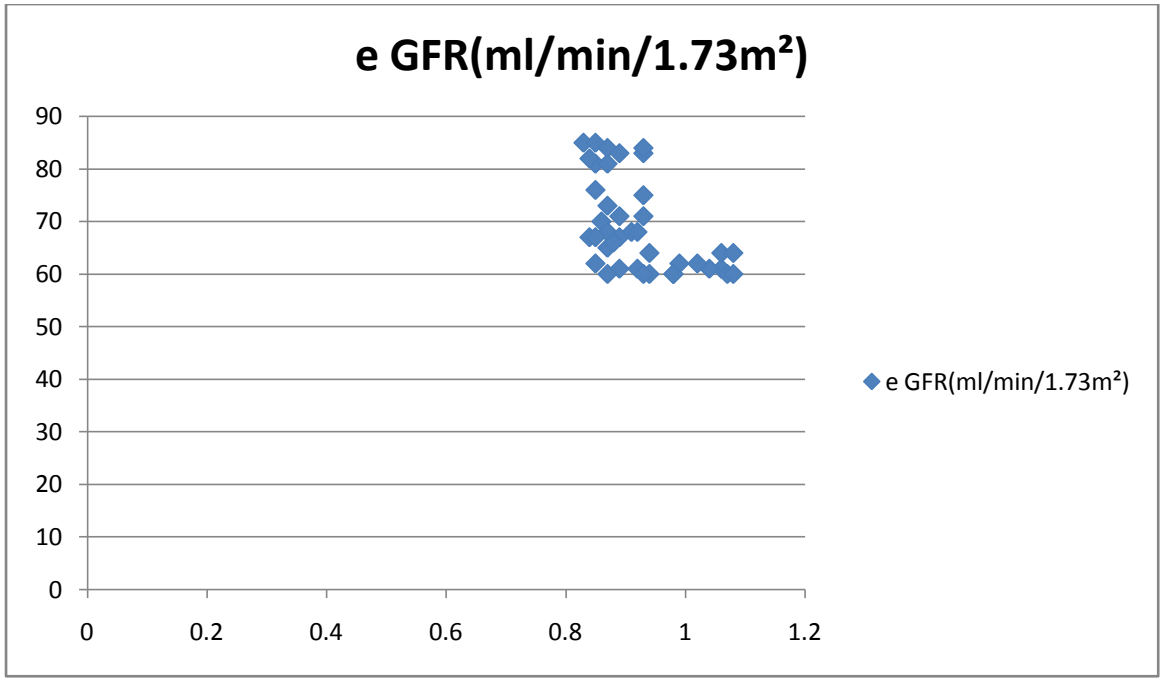

Figure – 24. Negative correlation of waist circumference with e GFR

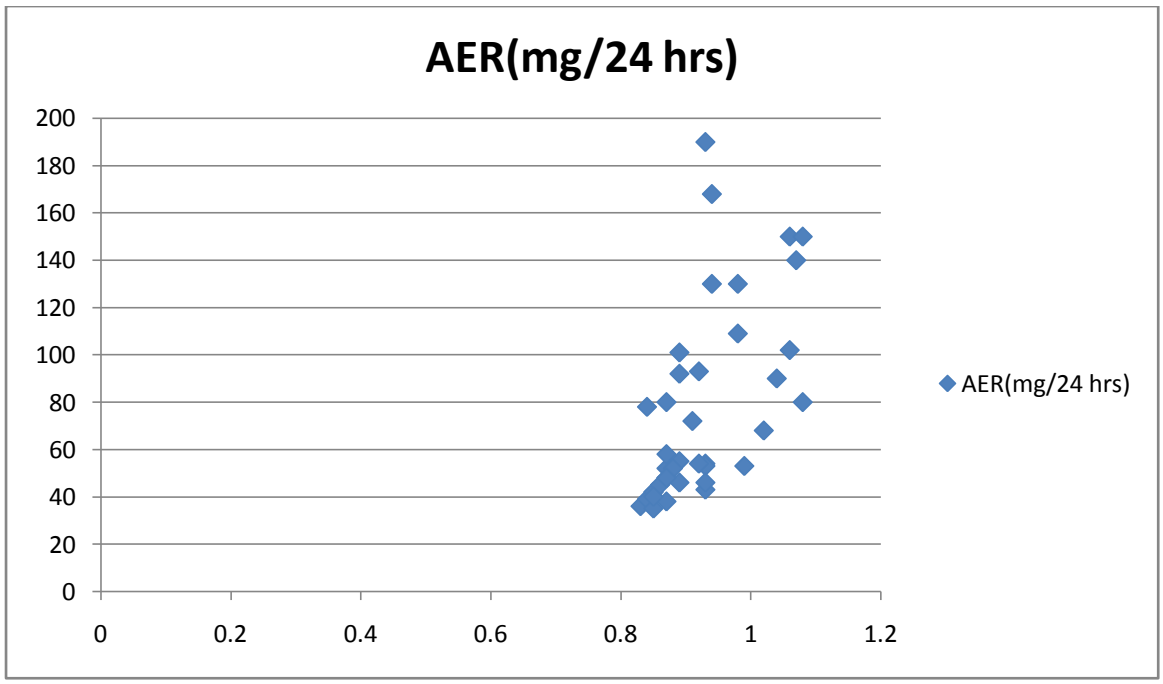

Figure – 25. Positive correlation of waist circumference with AER

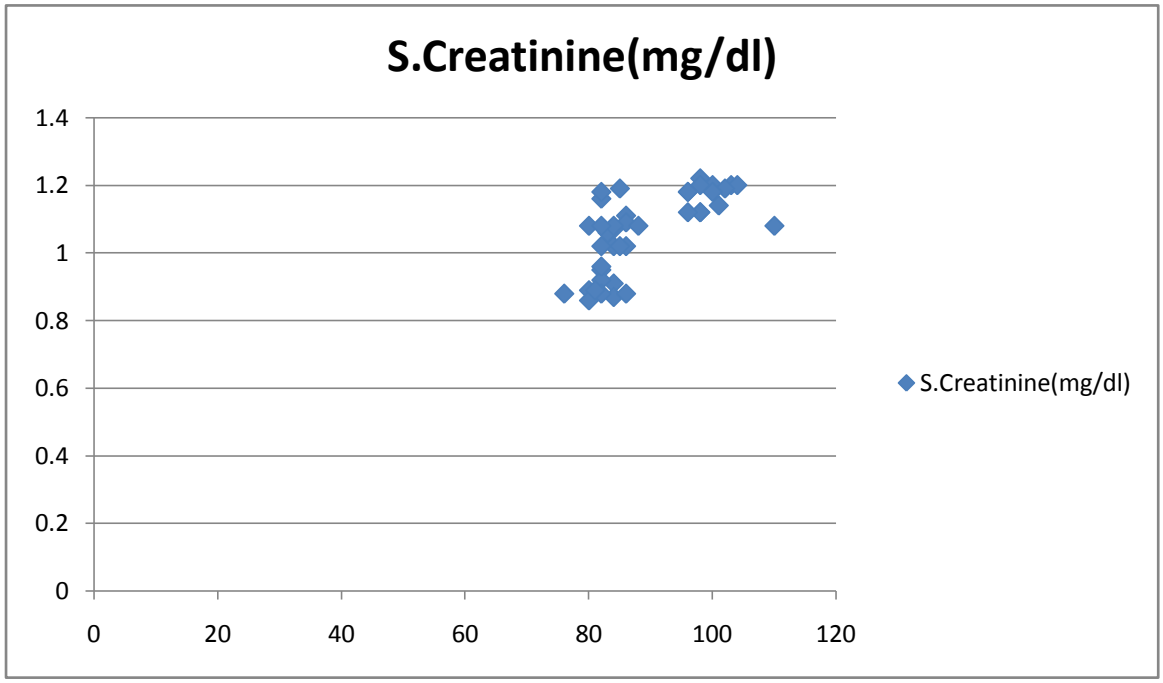

Figure – 26. Positive correlation of waist circumference with serum creatinine level

Table-15 & 16 and figures 24 – 26 show the correlation of WC with renal function decline of the study group consisted of stage 1-2 HT-CKD patients.Statistically significant negative correlation between WC with e GFR, positive correlation between WC and serum creatinine level and positive correlation between WC and AER were observed in the study group in this present study.

TABLE-17

STUDY GROUP (N=40)

Correlations of WHR with renal parameters

WHR	Correlation value	Statistical inference
CREAT(mg/dl)	**.507(**)**	**p<0.01 Significant**
e GFR (ml/min/1.73m^2)	**-.535(**)**	**p<0.01 Significant**
AER(mg/24 hrs)	**.601(**)**	**p<0.01 Significant**

** Correlation is significant at the 0.01 level

TABLE-18

STUDY GROUP (N=40)

Correlations of WHR with blood pressure & blood Urea level

WHR	Correlation value	Statistical inference
SBP(mmHg)	.230	p>0.05 Not Significant
DBP(mmHg)	.152	p>0.05 Not Significant
UREA(mg/dl)	.101	p>0.05 Not Significant

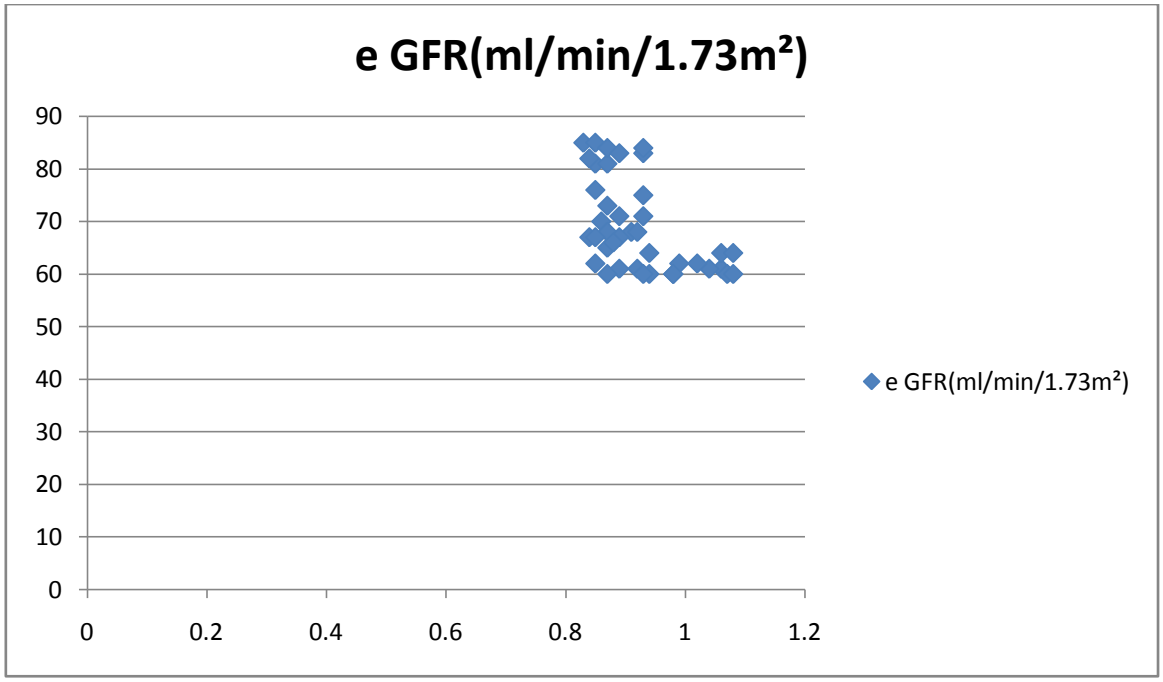

Figure – 27. Negative correlation of waist hip ratio with e GFR

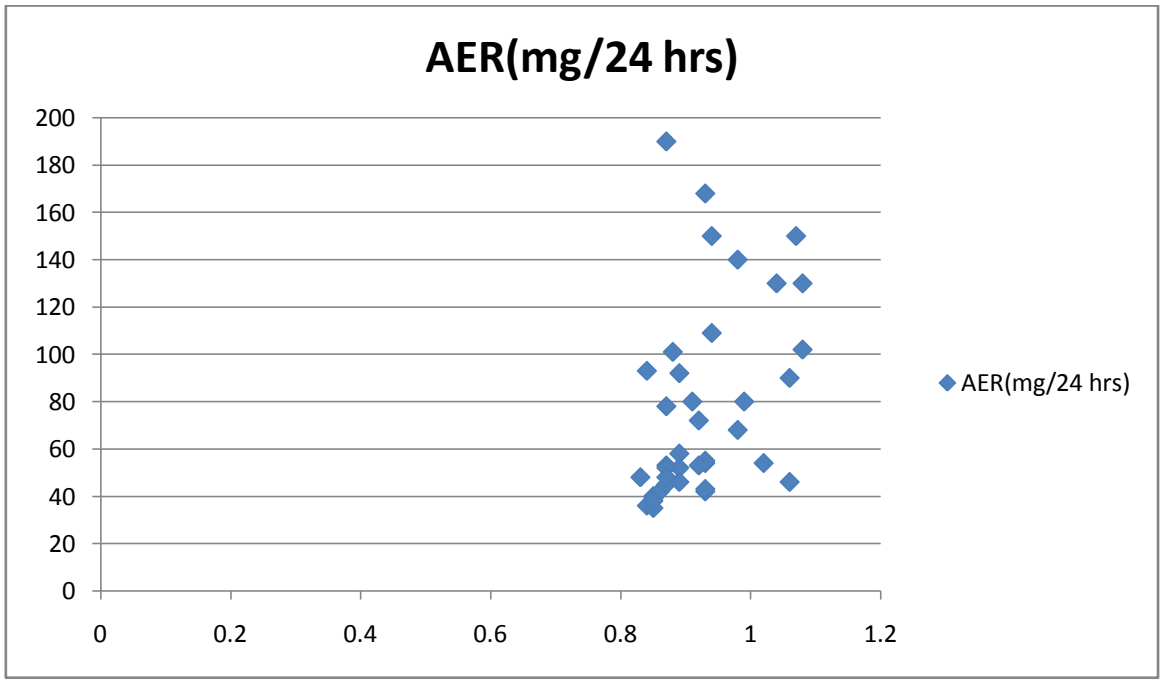

Figure – 28. Positive correlation of waist hip ratio with AER

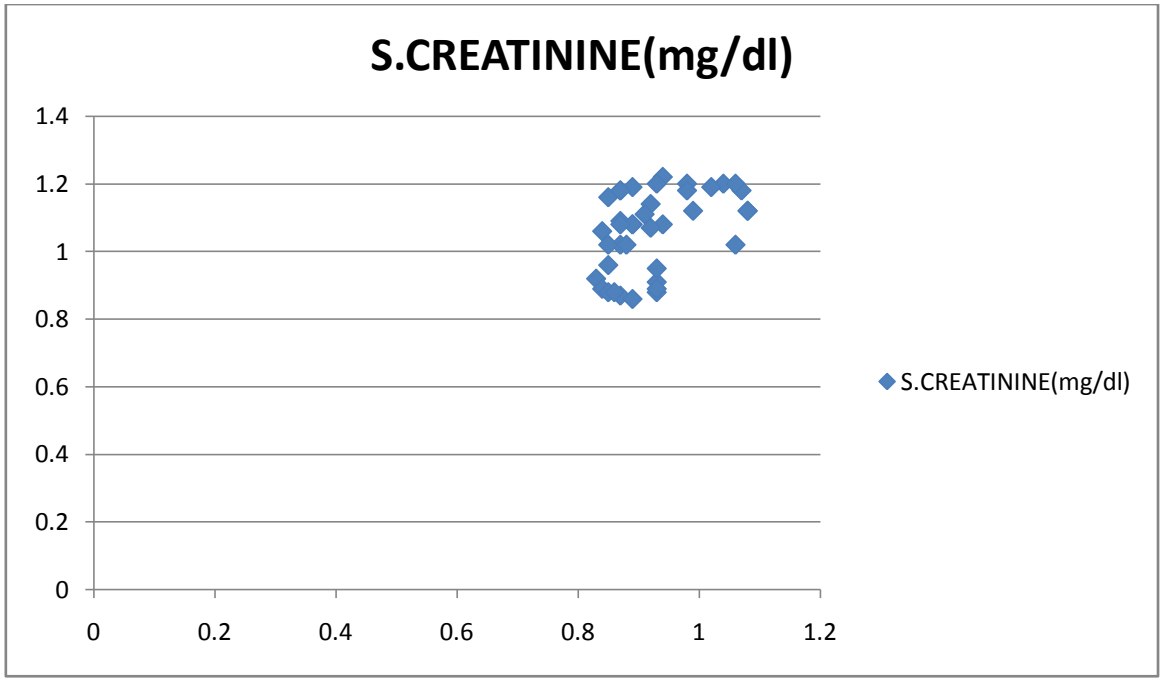

Figure – 29. Positive correlation of waist hip ratio with serum creatinine level

There are significant negative correlation between WHR and e GFR level , positive correlation between WHR and serum creatinine level and also positive correlation between WHR and AER level were observed in the study group and are represented in Tables-17 & 18 and Figures 27 – 29.

DISCUSSION

Obesity is a risk factor for cardiovascular diseases, hypertension, diabetes mellitus etc...But awareness of association between obesity and kidney damage is less.Prevalence of obesity is rapidly increasing now a days. Obesity is a chronic disorder that should be treated in a long term basis.

The main function of adipose tissue is the storage of triglyceride. Triglyceride is continuously redistributed in the adipose tissue and other parts of the body. Regional distribution of adipose tissue is important than the absolute amount of excess accumulation of adipose tissue.

Excess body fat accumulation accounts for 65 % - 75 % of essential hypertension.

In obesity, there is increased sympathetic nervous system activity, R-A-A-S activation, renal compression by accumulation of fat around the kidney. Increased adrenergic activity plays major role in the development of hypertension in obesity. Many factors are released by adipocytes such as,hormones-adiponectin,resistin,leptin,cytokines-TNF-α,IL-6,substrates-FFA,glycerol,enzymes-aromatase,complement factors-Factor-D,adipsin and also other Substances like PAI-1, angiotensinogen, RBP-4.These substances damage the peripheral tissues.

- Obesity → ↑ RPF → Glomerular hyperfiltration.
- Elevated systemic BP → transmitted to glomerulus → Glomerular hypertension → ↑ glomerular damage.

So both Hypertension and Obesity cause glomerular hyperfiltration which, over time lead to kidney damage.Obesity may directly cause a specific form of glomerulopathy (focal and segmental glomerulosclerosis).

Hallen et al [18] suggested ,elevated mean arterial pressure was an independent predictor of kidney function decline.

Klag et al [43] suggested elevated systolic bloodpressure was associated with elevated ESRD risk.

In our study, elevated level of both SBP and DBP were associated with kindey damage .

Weight loss is associated with decrease in bloodpressure.**Haynes et al** [66] and **Jones et al** [6] in their study they had proved it.

CKD is defined as progressive and irreversible renal function loss. There are five stages of CKD based on e GFR values.

CKD Stage I – II : e GFR ≥ 60 ml / min/1.73 m^2; UAC ≥ 30 – 299 mg / g (microalbuminuria) and ≥ 300 mg / g (macroalbuminuria).

CKD Stage III – IV : e GFR 15 – 59 ml / min / 1.73 m^2 .

Microalbuminuria not only indicates renal damage but is also an independent and well recognized marker of CKD progression.

Visceral / abdominal / central obesity is closely associated with renal damage when compared to high BMI.

Janssen et al [50] suggested that WC not the BMI was associated with obesity related health risk ,and in their study **Janssen et al** observed that WC was a better predictor of both abdominal and non-abdominal fat.

In our study, we observed that both high BMI and increased WC (visceral / central obesity) were associated with reduced renal function (reduced e GFR, elevated serum creatinine level,high AER,Blood Urea) ; but in high waist circumference more decline in kidney function was observed than other groups .

Hyunju Oh et al [49] **,Noori et al** [67] **,Elsayed et al** [68] in their study suggested that abdominal obesity was a better predictor and a major risk factor for renal function decline.

C Y Hsu et al [61] **, Vupputuri et al** [69] observed that BMI was associated with CKD in their studies.

Some other studies [67,70,71] reported BMI and Abdominal obesity both are risk factors for CKD.

Mahmoud et al [52] found that Abdominal obesity was strongly associated with microalbuminuria which is a better marker of renal damage.

In our study, there was strong statistically significant correlation of WC and WHR which are the indicators of central or abdominal obesity, with renal function reduction in stage I & II HT-CKD patients. And the correlation of BMI with kidney function decline was not statistically significant except reduction in e GFR .In our study, abdominal obesity was associated with renal function decline.

Pinto Sietsma et al [19] **,Knight EL et al** [72] **,Mulyadi et al** [73] ,in their study they suggested that microalbuminuria was associated with abnormal kidney function in non-diabetic individuals.

Some studies [74 – 76] suggested that there was no or inverse amount of BMI with e GFR decline.

Kitiyakara et al [76] in their study they observed WC was not associated with risk of CKD incidence.

Krammer et al [63] found incidence of CKD was higher in hypertensive patients with obesity than in hypertensive patients with normal weight.

Limitations of our study:

- Use of single measurement of creatinine
- Need of large sample size
- Absence of gold standard for body fat assessment (VFA)
- Need to follow for years to know further renal function decline due to the effect of central obesity.In our study both obesity and hypertension co-existed, so it is difficult to establish significance of these two in the development of kidney damage.

CONCLUSION

This case -control study was conducted between forty controls and forty patients with stage I-II chronic hypertensive kidney disease.

In our study, we found that abdominal obesity was statistically significantly correlated with renal function decline than increase in the BMI.

Abdominal obesity can be easily measured by simple methods like waist circumference, hip circumference and waist hip ratio with easily available instrument such as inch-tape .

The physicians can advice the obese patients to reduce the weight and suggest the patients that weight reduction can reduce the incidence of hypertension and their complications.

This study suggests, the importance of controlling the obesity, especially in hypertensive chronic kidney disease with initial stages of CKD and consequetively preventing the CKD progression.

We also suggests more specific measurement of central obesity like VFA (Visceral Fat Area) is needed for accurate correlation of central obesity with renal function decline. This study needs to be continued for years to assess the association of central obesity with faster renal decline.

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ABBREVIATIONS

WC –Waist circumference

BMI – Body mass index

Wt. –Weight

Ht.-Height

WHR –Waist Hip Ratio

SBP – Systolic blood pressure

DBP – Diastolic blood pressure

ESRD – End stage renal disease

NIH – National Institution of Health

ACR – Albumin creatinine ratio

HT-CKD – Hypertensive chronic kidney disease

GFR – Glomerular filtrate rate

TG – Triglycerides

VLDL – Very low density lipoprotein

FFA –Free fatty acid

HSL – Hormone sensitive lipase

WHO – World health organization

CART – Cocaine-and amphetamine-regulated transcript

POMC – Pro-opiomelanocortin

MCH – Melanin concentrating hormone

T_2DM – Type II diabetes mellitus

NKF-KD – National kidney foundation –kidney damage

MDRD –Modification of diet in renal disease

SNS – Sympathetic nervous system

R-A-A-S – Renin angiotensin aldosterone mechanism

VFA – Visceral Fat Area

PROFORMA

TOPIC: Effect of Body Mass Index and Waist circumference on renal function in Hypertensive Chronic Kidney Disease

Study Group/Control Group

Name: **Age:** **Sex:**

Address: **Occupation:**

H/O Present illness: changes in urine output, fatigue, weakness, swelling of feet and ankles

Past history: diabetes mellitus, hypertension, cardiovascular disease, surgeries

Personal history: smoking, alcohol, drug intake

Family history: h/o similar illness in the family members

Menstrual history:

General examination:

Height: Weight: Waist circumference:

Anaemic/Not Anaemic

Cyanosis/no cyanosis

Clubbing/No clubbing

Jaundice/No jaundice

Pedal edema/No pedal edema

Generalised lymphadenopathy present/absent

Vital signs: PR: BP: RR:

Examination of CVS:

Examination of RS:

Examination of Abdomen:

Examination of CNS:

Routine investigations:

Blood Urea: Serum Creatinine: Urine Albumin:

Urine Sugar:

RESULTS

PARAMETERS	BMI ($kg/m^{2)}$	WAIST CIRCUMF-ERENCE (cm)	BP (mmHg)	ALBUMIN EXCRETION RATE(mg/min)	BLOOD UREA (mg/dl)	SERUM CREATININE (mg/dL)	GFR (ml/min)
CONTROL							
HYPERTENSIVE CHRONIC KIDNEY DISEASE (STAGE I – II)							

INFORMED CONSENT

I understand the procedure and voluntarily agree to participate in this study, I also understand that this study is a noninvasive procedure and the possible adverse effects have been explained to me in details clearly in my own language.

Signature of the Subject

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

உயர் இரத்த அழுத்தம் சார்ந்த நீண்டகால சிறுநீரக நோய் உள்ளோர் மற்றும் ஆரோக்கியமான நபர்களுக்கும் இடையே உள்ள உடல் பருமன் அளவு மற்றும் இடுப்பு சுற்றளவு ஒப்பிடுதல்.

பெயர்: தேதி:

வயது: ஆராய்ச்சி சேர்க்கை எண்:

பாலினம்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களைப் பற்றி நான் புரிந்து கொண்டு எனது சம்மதம் தெரிவித்தேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

இந்த ஆராய்ச்சியினால் ஏற்படும் நன்மைகளையும் சில பக்க விளைவுகளையும் பற்றி தெளிவாக மருத்துவர் மூலம் தெரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழுசம்மதத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக் கொள்ள சம்மதிக்கிறேன

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள்:

இடம்:

<u>ஆராய்ச்சி தகவல் தாள்</u>

தஞ்சை மருத்துவக்கல்லூரி உடலியங்கியல் துறையில் உயர் இரத்த அழுத்தம் சார்ந்த நீண்டகால சிறுநீரக நோய் உள்ளோர்க்கும் மற்றும் ஆரோக்கியமான நபர்களுக்கும் உள்ள உடல்பருமன் அளவு மற்றும் இடுப்பு சுற்றளவுகளை ஒப்பிட்டு ஆய்வு மேற்கொள்ளப்படுகிறது.

இந்த ஒப்பீட்டு ஆய்வின் முடிவுகள் உயர் இரத்த அழுத்தம் சார்ந்த நீண்டகால சிறுநீரக நோய் உள்ளோர் மற்றும் பிறர்க்கும் இடையே உள்ள உடல்பருமன் அளவு மற்றும் இடுப்பு சுற்றளவு குறித்த வேறுபாடுகளை வெளிப்படுத்தும்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இரத்த பரிசோதனையின் முடிவுகள் ஆராய்ச்சியின்போதோ அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள்:

இடம்:

MASTER CHART														
S. NO	**Group**	AGE (yrs)	SBP (mmHg)	DBP (mmHg)	HEIGHT (meters)	WEIGHT (Kg)	BMI (Kg/m^2)	WC (cm)	HC (cm)	WHR	UREA (mg/dl)	CREAT (mg/dl)	e GFR ($ml/min/1.73m^2$)	AER (mg/24 hrs)
1	A	42	140	90	1.61	58	22.4	82	96	0.85	42	1.16	62	40
2	A	45	146	86	1.58	56	22.4	84	98	0.85	51	0.91	81	42
3	A	47	148	90	1.68	54	19.1	76	82	0.93	48	0.88	83	43
4	A	53	150	96	1.6	56	21.9	82	88	0.93	46	0.95	75	54
5	A	49	140	90	1.56	57	23.5	84	90	0.93	45	0.87	84	53
6	A	43	146	96	1.62	54	20.8	82	94	0.87	60	0.92	81	48
7	A	40	140	90	1.6	58	22.7	80	96	0.83	41	0.89	85	36
8	A	52	140	86	1.58	58	23.3	86	102	0.84	42	0.88	82	39
9	A	46	140	90	1.6	52	20.3	82	96	0.85	44	0.96	76	35
10	A	43	140	88	1.6	56	21.9	82	96	0.85	46	0.88	85	42
11	A	47	140	90	1.58	54	21.6	84	98	0.86	48	1.02	70	45
12	A	52	142	88	1.62	58	22.1	80	92	0.87	52	0.86	84	52
13	A	45	140	90	1.65	58	21.3	81	91	0.89	51	0.89	83	55
14	A	45	146	92	1.62	59	22.5	82	88	0.93	53	1.02	71	46

15	A	42	140	86	1.58	56	22.4	96	90	1.06	46	1.18	61	150
16	A	40	140	90	1.6	58	22.6	103	96	1.07	58	1.2	60	140
17	A	42	140	96	1.62	58	22.1	104	106	0.98	49	1.2	60	130
18	A	39	150	90	1.65	58	21.5	100	98	1.04	62	1.2	61	90
19	A	44	140	90	1.58	56	22.4	98	100	1.06	57	1.12	64	102
20	A	43	150	90	1.56	58	24.2	98	100	1.08	56	1.12	64	80
21	A	45	140	90	1.52	56	24.3	101	102	0.99	52	1.14	62	53
22	A	41	140	96	1.6	58	22.6	102	110	0.92	48	1.19	61	54
23	A	39	150	92	1.5	56	24.8	100	100	1.02	44	1.18	62	68
24	A	38	140	90	1.54	58	24.4	98	100	0.98	46	1.22	60	109
25	A	44	140	92	1.58	58	23.2	96	102	0.94	47	1.12	64	130
26	A	42	142	90	1.62	60	22.9	110	101	1.08	42	1.08	60	150
27	A	41	140	90	1.58	58	23.2	98	104	0.94	49	1.2	60	168
28	A	46	130	86	1.6	59	23	96	103	0.93	52	1.18	60	190
29	A	44	140	86	1.54	68	28.7	86	98	0.87	58	1.11	65	80
30	A	43	136	92	1.6	70	27.3	84	92	0.91	61	1.07	68	72
31	A	44	146	88	1.58	68	27.2	83	90	0.92	62	1.06	68	93

32	A	42	140	88	1.64	72	26.8	86	102	0.84	46	1.09	67	78
33	A	39	140	90	1.62	66	25.2	84	96	0.87	51	1.08	68	58
34	A	44	140	90	1.62	70	26.7	88	98	0.89	52	1.08	67	46
35	A	41	148	90	1.52	60	26.1	85	95	0.89	55	1.19	61	92
36	A	46	146	86	1.6	68	26.6	86	96	0.89	56	1.02	71	101
37	A	47	140	90	1.58	65	26	80	90	0.88	58	1.08	66	52
38	A	47	140	88	1.52	59	25.6	82	94	0.87	61	1.18	60	48
39	A	40	140	90	1.6	73	28.5	85	97	0.87	49	1.02	73	38
40	A	43	140	90	1.56	64	26.3	82	96	0.85	58	1.08	67	40

GROUP A : STUDY GROUP

GROUP B : CONTROL GROUP

MASTER CHART														
S. NO	**Group**	AGE (yrs)	SBP (mmHg)	DBP (mmHg)	HEIGHT (meters)	WEIGHT (Kg)	BMI (Kg/m^2)	WC (cm)	HC (cm)	WHR	UREA (mg/dl)	CREAT (mg/dl)	e GFR ($ml/min/1.73m^2$)	AER (mg/24 hrs)
1	B	52	120	80	1.61	58	22.4	82	88	0.93	20	0.4	203	4.7
2	B	48	110	82	1.58	56	22.4	84	86	0.98	28	0.45	180	4.8
3	B	42	116	80	1.64	64	23.8	82	92	0.89	22	0.46	181	6
4	B	46	122	84	1.57	60	24.4	82	80	1.02	26	0.49	165	7.8
5	B	43	110	80	1.6	56	21.9	81	83	0.97	20	0.52	156	6
6	B	46	120	78	1.71	60	20.5	83	85	0.98	25	0.49	165	8
7	B	44	120	80	1.58	56	22.4	84	86	0.98	16	0.58	137	3.4
8	B	42	130	80	1.6	58	22.6	82	80	1.02	24	0.59	135	11
9	B	45	120	80	1.7	55	19	86	86	0.96	26	0.48	170	13
10	B	41	120	76	1.6	52	20.3	76	76	0.86	22	0.57	142	9
11	B	45	110	84	1.61	58	22.6	82	82	0.95	20	0.62	126	4.6
12	B	52	120	82	1.62	54	21.1	78	78	0.97	22	0.49	161	4.4
13	B	44	120	80	1.56	57	23.7	85	85	0.98	18	0.62	127	12

14	B	43	130	80	1.6	58	22.6	86	86	0.95	30	0.63	125	10
15	B	47	120	82	1.58	52	20.8	80	80	0.93	24	0.54	147	1.9
16	B	42	118	84	1.62	56	21.8	86	86	0.97	26	0.72	108	3.8
17	B	43	116	78	1.64	58	22.1	85	85	0.94	32	0.4	217	6
18	B	48	120	82	1.68	60	2.3	82	82	0.89	20	0.69	110	7
19	B	42	120	80	1.59	56	22.2	81	81	0.9	18	0.62	128	4.1
20	B	52	120	80	1.64	58	21.5	86	86	0.96	16	0.42	192	4.8
21	B	49	110	70	1.71	58	20.07	82	82	0.93	18	0.56	139	9.8
22	B	42	110	80	1.6	56	21.9	81	81	0.92	22	0.68	115	5.6
23	B	49	100	76	1.58	58	23.3	83	83	1.01	24	0.63	122	5.5
24	B	52	110	80	1.64	56	20.8	80	80	0.94	26	0.72	103	16
25	B	45	120	82	1.68	56	19.86	78	78	0.95	18	0.66	117	2.8
26	B	52	110	70	1.56	57	23.5	82	82	0.95	23	0.53	147	5
27	B	49	100	76	1.52	54	23.4	85	85	0.96	20	0.59	131	8.2
28	B	48	106	76	1.6	56	21.1	80	89	0.89	18	0.64	120	14
29	B	47	110	74	1.58	54	21.6	82	86	0.95	20	0.59	132	7.1
30	B	38	120	80	1.6	58	22.7	82	88	0.93	22	0.73	108	2.5

31	B	44	126	80	1.72	58	19.6	82	90	0.89	16	0.67	116	3.9
32	B	49	120	76	1.52	54	23.4	83	80	1.03	19	0.48	167	6.7
33	B	52	120	80	1.64	52	22.6	82	85	0.96	24	0.56	138	4.2
34	B	48	116	78	1.58	52	19.3	82	86	0.95	22	0.64	120	1.7
35	B	41	118	80	1.6	50	19.5	80	88	0.9	20	0.68	116	3.7
36	B	48	112	80	1.51	52	20.8	82	92	0.89	18	0.56	140	5.6
37	B	43	116	72	1.68	54	19.1	78	90	0.86	26	0.63	125	4.8
38	B	47	120	80	1.62	54	20.8	85	89	0.95	12	0.63	123	9.6
39	B	52	126	80	1.56	52	21.7	82	98	0.83	14	0.62	123	5.5
40	B	49	130	76	1.58	50	20	80	96	0.83	16	0.71	106	2.4

GROUP A : STUDY GROUP

GROUP B : CONTROL GROUP

HT-CKD						HT-CKD						HT-CKD					
BMI(Kg/m^2)						e GFR(ml/min/1.73m^2)						AER(mg/24 hrs)					
GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3	
A1	22.4	A15	22.4	A29	28.7	A1	62	A15	61	A29	65	A1	40	A15	150	A29	80
A2	22.4	A16	22.6	A30	27.3	A2	81	A16	60	A30	68	A2	42	A16	140	A30	72
A3	19.1	A17	22.1	A31	27.2	A3	83	A17	60	A31	68	A3	43	A17	130	A31	93
A4	21.9	A18	21.5	A32	26.8	A4	75	A18	61	A32	67	A4	54	A18	90	A32	78
A5	23.5	A19	22.4	A33	25.2	A5	84	A19	64	A33	68	A5	53	A19	102	A33	58
A6	20.8	A20	24.2	A34	26.7	A6	81	A20	64	A34	67	A6	48	A20	80	A34	46
A7	22.7	A21	24.3	A35	26.1	A7	85	A21	62	A35	61	A7	36	A21	53	A35	92
A8	23.3	A22	22.6	A36	26.6	A8	82	A22	61	A36	71	A8	39	A22	54	A36	101
A9	20.3	A23	24.8	A37	26	A9	76	A23	62	A37	66	A9	35	A23	68	A37	52
A10	21.9	A24	24.4	A38	25.6	A10	85	A24	60	A38	60	A10	42	A24	109	A38	48
A11	21.6	A25	23.2	A39	28.5	A11	70	A25	64	A39	73	A11	45	A25	130	A39	38
A12	22.1	A26	22.9	A40	26.3	A12	84	A26	60	A40	67	A12	52	A26	150	A40	40
A13	21.3	A27	23.2			A13	83	A27	60			A13	55	A27	168		
A14	22.5	A28	23			A14	71	A28	60			A14	46	A28	190		

HT-CKD						HT-CKD						HT-CKD					
WC(cm)						WHR						UREA(mg/dl)					
GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3	
A1	82	A15	96	A29	86	A1	0.85	A15	1.06	A29	0.87	A1	42	A15	46	A29	58
A2	84	A16	103	A30	84	A2	0.85	A16	1.07	A30	0.91	A2	51	A16	58	A30	61
A3	76	A17	104	A31	83	A3	0.93	A17	0.98	A31	0.92	A3	48	A17	49	A31	62
A4	82	A18	100	A32	86	A4	0.93	A18	1.04	A32	0.84	A4	46	A18	62	A32	46
A5	84	A19	98	A33	84	A5	0.93	A19	1.06	A33	0.87	A5	45	A19	57	A33	51
A6	82	A20	98	A34	88	A6	0.87	A20	1.08	A34	0.89	A6	60	A20	56	A34	52
A7	80	A21	101	A35	85	A7	0.83	A21	0.99	A35	0.89	A7	41	A21	52	A35	55
A8	86	A22	102	A36	86	A8	0.84	A22	0.92	A36	0.89	A8	42	A22	48	A36	56
A9	82	A23	100	A37	80	A9	0.85	A23	1.02	A37	0.88	A9	44	A23	44	A37	58
A10	82	A24	98	A38	82	A10	0.85	A24	0.98	A38	0.87	A10	46	A24	46	A38	61
A11	84	A25	96	A39	85	A11	0.86	A25	0.94	A39	0.87	A11	48	A25	47	A39	49
A12	80	A26	110	A40	82	A12	0.87	A26	1.08	A40	0.85	A12	52	A26	42	A40	58
A13	81	A27	98			A13	0.89	A27	0.94			A13	51	A27	49		
A14	82	A28	96			A14	0.93	A28	0.93			A14	53	A28	52		

HT-CKD						HT-CKD						HT-CKD					
CREAT(mg/dl)						SBP(mmHg)						DBP(mmHg)					
GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3		GROUP-1		GROUP-2		GROUP-3	
A1	1.16	A15	1.18	A29	1.11	A1	140	A15	140	A29	140	A1	90	A15	86	A29	86
A2	0.91	A16	1.2	A30	1.07	A2	140	A16	146	A30	136	A2	86	A16	90	A30	92
A3	0.88	A17	1.2	A31	1.06	A3	140	A17	148	A31	146	A3	90	A17	96	A31	88
A4	0.95	A18	1.2	A32	1.09	A4	150	A18	150	A32	140	A4	96	A18	90	A32	88
A5	0.87	A19	1.12	A33	1.08	A5	140	A19	140	A33	140	A5	90	A19	90	A33	90
A6	0.92	A20	1.12	A34	1.08	A6	150	A20	146	A34	140	A6	96	A20	90	A34	90
A7	0.89	A21	1.14	A35	1.19	A7	140	A21	140	A35	148	A7	90	A21	90	A35	90
A8	0.88	A22	1.19	A36	1.02	A8	140	A22	140	A36	146	A8	86	A22	96	A36	86
A9	0.96	A23	1.18	A37	1.08	A9	150	A23	140	A37	140	A9	90	A23	92	A37	90
A10	0.88	A24	1.22	A38	1.18	A10	140	A24	140	A38	140	A10	88	A24	90	A38	88
A11	1.02	A25	1.12	A39	1.02	A11	140	A25	140	A39	140	A11	90	A25	92	A39	90
A12	0.86	A26	1.08	A40	1.08	A12	142	A26	142	A40	140	A12	88	A26	90	A40	90
A13	0.89	A27	1.2			A13	140	A27	140			A13	90	A27	90		
A14	1.02	A28	1.18			A14	130	A28	146			A14	92	A28	86		